Title: Classification, diagnosis and prognosis of acute myeloid leukemia by gene expression profiling.

TECHNICAL FIELD

The present invention is in the field of medicine. The invention relates in particular to methods of genetic analysis for the classification, diagnosis and prognosis of acute myeloid leukemia. Also, the invention relates to nucleic acid expression profiles as obtained from cells of AML patients, which profiles by similarity group into a plurality of distinct and defined clusters that characterize different classes of AML. The invention relates to the use of such expression profiles and compositions in diagnosis and therapy of AML and specifically in the prediction of prognostically important AML classes.

The invention further relates to methods for the diagnosis of AML and for the determination of the prognosis of a subject affected by AML and to kits of parts comprising sets of nucleic acid probes suitable for performing methods of the invention either by means of genomics or proteomics.

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BACKGROUND OF THE INVENTION

Acute myeloid leukemia (AML) is a collection of neoplasms with heterogeneous pathophysiology, genetics and prognosis. Based on cytogenetics and molecular analysis, AML patients are presently classified into groups or subsets of AML with markedly contrasting prognosis. For instance, the genetic translocations inv(16), t(8;21) and t(15;17) characterize AML with a relatively favourable prognosis, whereas the cytogenetically bad-risk leukemia's include patients with abnormalities involving 11q23, loss of 5(q) or 7(q), t(6;9) and t(9;22) (Löwenberg et al., 1999).

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The most common molecular abnormality in AML is the internal tandem duplication (ITD) in the fms-like tyrosine kinase-3 gene (FLT3), a hematopoietic growth factor receptor (Levis & Small, 2003). FLT3 ITD

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mutations confer a bad prognosis to AML patients (Levis & Small, 2003). AML patients with mutations in the transcription factor cEBPα have been associated with good outcome (Preudhomme et al., 2002; van Waalwijk van Doorn-Khosrovani et al., 2003), while elevated expression of the transcription factor EVI1 predicts for notoriously poor survival (van Waalwijk van Doorn-Khosrovani et al., 2003). These examples of novel molecular prognostic markers underscore the importance of an extension of molecular analyses in AML.

Approximately thirty percent of all patients with acute myeloid leukemia (AML) are currently classified based on specific abnormal karyotypes in groups with either good or bad prognosis. The remaining seventy percent of patients, however, are not classifiable because of the lack of cytogenetic markers.

One of the aims of the present invention is to provide more accurate risk assessment tools for the diagnosis of AML. It is another aim to classify AML patients in which specific abnormal karyotypes have not been found and to distinguish these groups not only from the molecularly well-defined AML classes, but also to define prognostic subgroups within these unclassified AML types. The presence of additional prognostic classes in AML, not recognizable with currently available methods, may provide important insights into their pathophysiology. Therefore, it is an aim of the present invention to provide a more complete way of prognostication to patients with AML.

SUMMARY OF THE INVENTION

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The present invention is based on the discovery that unique correlations within gene expression profiles and also with cytogenetic aberrations can be recognized with high accuracy within a representative cohort of AML patients. It has for instance been found that gene expression profiles obtained from a large number of AML patients can be clustered according to similarity. This enables the recognition of distinct classes of AML

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with similar expression profiles characterising such a class. It was thus found that AML could be classified into distinct subclasses, each subclass being characterised by a specific clustering of gene expression profiles. Further it was found that truly discriminative genes for most of these classes or clusters could be identified, a cluster for instance being characterized therein that the expression of multiple genes is up-regulated or down-regulated in that cluster whereas their expression in another cluster is unaffected.

Based on these findings, the present invention now provides in a first aspect a method for producing a classification scheme for AML comprising the steps of:

- a) providing a plurality of reference samples, said reference samples comprising cell samples from a plurality of reference subjects affected by AML;
- b) providing reference profiles by establishing a gene expression profile for each of said reference samples individually;
- c) clustering said individual reference profiles according to similarity, and
- d) assigning an AML class to each cluster.

In a preferred embodiment of such a method, the clustering of reference profiles is performed based on the information of genes that are differentially-expressed between profiles, and in an even more preferred embodiment of such a method, the clustering of said reference profiles is performed on the basis of the information of the genes of table 1, still more preferably of the genes of table 2, which tables are provided hereinbelow. In a further aspect, the present invention provides a method for classifying the

- AML of an AML affected subject, comprising the steps of:
 - a) providing a classification scheme for AML by producing such a scheme according to the method of any one of claims 1-3;
 - b) providing a subject profile by establishing a gene expression profile for said subject;
 - c) clustering the subject profile together with the reference profiles;

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d) determining in said scheme the clustered position of said subject profile among the reference profiles, and

e) assigning to said AML of said subject the AML class that corresponds to said clustered position in case said subject profile is within any cluster of reference profiles, or assigning to said AML of said subject a new AML class.

In yet a further aspect, the present invention provides a method for diagnosing AML in an AML affected subject comprising:

- a) producing a classification scheme for AML according to a method of the invention;
- b) defining cluster-specific genes for each cluster by selecting those genes of which the expression level characterizes the clustered position of the corresponding AML class among the various AML classes within said scheme;
- c) determining the level of expression of a sufficient number of said cluster- specific genes in an AML affected subject;
- d) establishing whether the level of expression of said cluster-specific genes in said subject shares sufficient similarity to the level of expression that characterizes an individual AML class to thereby determine the presence of AML corresponding to said class in said subject.

In one embodiment of such a method for diagnosing AML, said cluster-specific genes may comprise all genes comprised in said gene expression profile. In a preferred embodiment of such a method, said cluster-specific genes comprise a set of 1 to 3000 genes of the genes of table 1, more preferably 1 to 600 genes of the genes of table 1, still more preferably 1 to 50 genes of the genes of table 1. In an even more preferred embodiment said cluster-specific genes comprise a set of 1 to 600 genes of the genes of table 2, still more preferably 1 to 50 genes of the genes of table 2, and even more preferably 1 to 25 genes of the genes of table 2. Most preferred in such a

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method is the use of the differentially-expressed genes as shown in Table 3 for the diagnosis of a specific AML class in a subject.

In yet another aspect, the present invention provides a method of determining the prognosis for an AML affected subject, said method comprising the steps of:

- a) providing a classification scheme for AML by producing such a scheme according to a method of the invention;
- b) determining the prognosis for each AML class in said scheme based on clinical records for the AML subjects comprised in said class;
- c) establishing the AML class of an AML affected subject by diagnosing and/or classifying AML in said subject according to a method of the invention, and
- d) assigning to said subject the prognosis corresponding to the established AML class of said AML affected subject.

The present invention further provides a classification scheme for AML, said scheme comprising a plurality of distinct AML classes that are differentiated on the basis of similarity clustering of gene expression profiles obtained from a plurality of reference subjects affected by AML.

Said classification scheme is for instance obtainable by a method of the invention for producing such a scheme. Preferably, said classification scheme is obtained by a method involving K-means clustering of gene expression profiles based on, for instance, gene chip array-acquired values for hybridization intensities for each gene, such as for instance those obtainable by using an Affymetrix gene chip.

Analysis of gene expression profiles obtained by using such gene chips preferably involves log 2 transformation of all intensity values in order to detect subtle modulations between the various genes. For each gene the geometric mean (i.e. the mean expression value determined for all individual genes in all profiles to be analysed) is calculated. Deviation from this geometric mean is termed differential expression. Genes that are expressed at values

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allowing assignment of being differentially-expressed are used for hierarchical clustering. Subsequently the gene signatures (characteristic expression profiles) of all samples/patients are compared with each other by means of a Pearson correlation coefficient analysis showing the (pathway) resemblance within clinical distinct groups of the total patient population.

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The present invention further provides genes that are modulated (up- and down-regulated) in AML compared to the geometric mean calculated from all patients. Such genes and the proteins they encode are useful for diagnostic and prognostic purposes, and may also be used as targets for screening therapeutic compounds that modulate AML, such as antibodies. The methods of detecting nucleic acids of the invention or their encoded proteins can be used for a number of purposes. Examples include early detection of AML, monitoring and early detection of relapse following treatment of AML, monitoring response to therapy of AML, determining prognosis of AML, directing therapy of AML, selecting patients for postoperative chemotherapy or radiation therapy, selecting therapy, determining tumor prognosis, treatment, or response to treatment, and early detection of precancerous condition. Other aspects of the invention will become apparent to the skilled artisan by the following description of the invention.

In one aspect, the present invention provides a method of detecting an AML-associated transcript in one or more cells from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide, such as an oligonucleotide, that selectively hybridizes to a sequence at least 80% identical to a sequence of a gene as shown in Tables 1 or 2. In one embodiment, the polynucleotide selectively hybridizes to a sequence at least 95% identical to a sequence of a gene as shown in Tables 1 or 2. In another embodiment, the polynucleotide comprises a sequence of a gene as shown in Tables 1 or 2.

In one embodiment, the biological sample used in such methods of detection is a tissue sample. In another embodiment, the biological sample

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comprises isolated nucleic acids, e.g., mRNA. In one embodiment, the polynucleotide is labeled, e.g., with a fluorescent label. In one embodiment, the polynucleotide is immobilized on a solid surface.

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DESCRIPTION OF THE DRAWINGS

Figure 1 shows, in panel (A), a Correlation View of 286 AML patients. The Correlation Visualization tool displays pair-wise correlations between the samples. The patient samples in the visualization are colored by Pearson's correlation coefficient values with deeper colors indicating higher positive (red) or negative (blue) correlations, indicating similarity in the underlying pathway indicative for the subgroups reflecting the heterogeneity within the patient population. The scale bar indicates 100% correlation (red) towards 100% anti correlation (blue). In order to reveal correlation patterns, a matrix ordering method is applied to rearrange the samples. The ordering algorithm starts with the most correlated sample pair and, through an iterative process, sorts all the samples into correlated blocks. Each sample is joined to a block in an ordered manner so that a correlation trend is formed within a block with the most correlated samples at the centre. The blocks are then positioned along the diagonal of the plot in a similar ordered manner.

Panel (B) of Figure 1 shows an adapted Correlation View of 286 AML patients (right panel) and top40 genes defining the 16 individual clusters of patients (left panel). All 16 clusters identified on the basis of the Correlation View are indicated (1 to 16). FAB classification and karyotype based on cytogenetics are depicted in the columns along the original diagonal of the Correlation View (FAB M1-green, M2-purple, M3-orange, M4-yellow, M5-blue, M6-grey; karyotype: normal-green, inv(16)-yellow, t(8;21)-purple, t(15;17)-orange, 11q23 abnormalities-blue, other-grey). FLT3 ITD, FLT3 TKD, N-RAS, K-RAS and cEBPα mutations and EVI1 overexpression are depicted in the same set of columns (red bar: positive and green bar: negative). The expression

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levels of the top 40 genes identified by Significance Analysis of Microarrays (SAM) analyses of each of the 16 clusters are visualized in the left panel. The scale bar indicates 4-fold upregulation (red) towards 4-fold downregulation (green) relative to the geometric mean of all samples.

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Figure 2 shows the overall survival (panel A), event free survival (panel B) and relapse rate after CR (panel C) of AML patients in cluster #5 (M4/M5), cluster #9 (inv(16)), cluster #10 (EVII/monosomy 7), cluster #12 (t(15;17)) and cluster #13 (t(8;21)), indicating that expression profiles in acute myeloid leukemia associate with diverse genetic aberrations and have prognostic impact.

Figure 3 provides a guideline on how to read the Omniviz Correlation View. The figure shows the Correlation View and FAB classification (right-hand edge of figure) of the cohort of 286 AML patients (2856 probe sets). A total of 16 distinct cluster can be identified on the right edge of the figure. X-axis and Y-axis show the regions of the various clusters 1-16 from top to bottom and from left to right, respectively. An exemplary correlation between cluster #5 and #16 is indicated by rectangle. Both clusters predominantly consist of AML-M5 (not visible) and correlate. However, they do form separate clusters. Anti-correlation for instance between cluster 5 and cluster #13, which merely contains AML-M2, is indicated by the dashed rectangle. Correlation and anti-correlation between every individual (sub)cluster can be extracted from the Correlation View and (sub)clusters can subsequently be assigned, e.g., cluster #6, #7 and #8 (dotted lines). FAB: M0-bright green, M1-green, M2-pink, M3-orange, M4-purple, M5-turquoise, M6-yellow (with number).

Figures 4-10 provide supporting results of the Pearson's correlation coefficient analyses using Omniviz with different probe subsets. In the Correlation View all 286 patients are plotted against all 286 AML patients. FAB classification and karyotype based on cytogenetics are depicted in the columns along the original diagonal (left-hand edge) of the Correlation View

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(FAB M0-red, M1-green, M2-purple, M3-orange, M4-yellow, M5-blue, M6-grey; karyotype: normal-green, inv(16)-yellow, t(8;21)-purple, t(15;17)-orange, 11q23 abnormalitiesblue, 7(q) abnormalities-red, +8-pink, complex-black, other-grey). *FLT3* ITD, *FLT3* TKD, N-RAS, K-RAS and cEBP α mutations and EVT1 overexpression are depicted in the same set of columns (red bar: positive and green bar: negative). Figure 4: 147 probe; Figure 5: 293 probe sets; Figure 6: 569 probe sets; Figure 7: 984 probe sets; Figure 8: 1692 probe sets; Figure 9: 2856 probe sets; Figure 10: 5071 probe sets.

Figure 11 shows the Southern blot analyses AML patients with cryptic inv(16). Southern blot analyses was carried out with a myosine heavy chain 11 specific probe (NT 010393, 136753-137404 nt) on material of AML (WT, no inv(16)), AML with known inv(16) breakpoint (type A and E) and three patients that clustered with all known AML and inv(16) patients in the Correlation View (Figure 1).

Figure 12 shows the Expression of *MYH11* as determined by Affymetrix GeneChip analyses in 286 cases of AML and controls. Expression levels of *MYH11* were high in AML patients and inv(16), whereas low levels were detected in the other AML patients, CD34-positive cells and normal bone marrow.

Figure 13 shows a snapshot of Correlation View showing the AML-M3 t(15;17) patients. FAB M2-purple, M3-orange, M4-yellow. Karyotype: normal-green, t(15;17)-orange, other-grey. The AML-M3 t(15;17) patients are divided into two groups, i.e., low white blood cell count (WBC) and FLT3 ITD negative (green bar) versus high WBC/FLT3 ITD positive (red bar). Karyotype is based on cytogenetics and WBC is depicted as 10 (cells/l).

Figure 14 shows the Expression of *ETO* as determined by Affymetrix GeneChip analyses in 286 cases of AML and controls. Expression levels of *ETO* were high in AML patients and t(8;21), whereas low levels were detected in the other AML patients, CD34-positive cells and normal bone marrow.

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DETAILED DESCRIPTION OF THE INVENTION

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The term "classifying" is used in its art-recognized meaning and thus refers to arranging or ordering items, *i.c.* gene expression profiles, by classes or categories or dividing them into logically hierarchical classes, subclasses, and sub-subclasses based on the characteristics they have in common and/or that distinguish them. In particular "classifying" refers to assigning, to a class or kind, an unclassified item. A "class" then being a grouping of items, based on one or more characteristics, attributes, properties, qualities, effects, parameters, etc., which they have in common, for the purpose of classifying them according to an established system or scheme.

The term "classification scheme" is used in its art-recognized meaning and thus refers to a list of classes arranged according to a set of preestablished principles, for the purpose of organizing items in a collection or into groups based on their similarities and differences.

The term "clustering" refers to the activity of collecting, assembling and/or uniting into a cluster or clusters items with the same or similar elements, a "cluster" referring to a group or number of the same or similar items, *i.c.* gene expression profiles, gathered or occurring closely together based on similarity of characteristics. "Clustered" indicates an item has been subjected to clustering.

The term "clustered position" refers to the location of an individual item, *i.c.* a gene expression profile, in amongst a number of clusters, said location being determined by clustering said item with at least a number of items from known clusters.

The process of clustering used in a method of to the present invention may be any mathematical process known to compare items for similarity in characteristics, attributes, properties, qualities, effects, parameters, etc.. Statistical analysis, such as for instance multivariance analysis, or other methods of analysis may be used. Preferably methods of analysis such as self-organising maps, hierarchical clustering,

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multidimensional scaling, principle component analysis, supervised learning, k-nearest neighbours, support vector machines, discriminant analyse, partial least square methods and/or Pearson's correlation coefficient analysis are used. In another preferred embodiment of a method of the present invention Pearson's correlation coefficient analysis, significance analysis of microarrays (SAM) and/or prediction analysis of microarrays (PAM) are used to cluster gene expression profiles according to similarity. A highly preferred method of clustering comprises similarity clustering of gene expression profiles wherein the expression level of differentially-expressed genes, having markedly lower or higher expression than the geometric mean expression level determined for all genes in all profiles to be clustered, is log(2) transformed, and wherein the transformed expression levels of all differentially-expressed genes in all profiles to be clustered is clustered by using K-means. A numerical query may then be used to select a subset of genes used in the process of hierarchical clustering (Eisen et al., 1998), thus, numerical queries may be run to select differentially expressed genes relative to the calculated geometric mean to select a smaller group of genes for hierarchical clustering.

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Unsupervised sample clustering using genes obtained by numerical or threshold filtering is used to identify discrete clusters of samples as well as the gene-signatures associated with these clusters. The term gene signatures is used herein to refer to the set of genes that define the discrete position of the cluster apart from all other clusters, and includes cluster-specific genes. A numerical or threshold filtering is used to select genes for the analysis that are most likely of diagnostic relevance. Hierarchical clustering allows for visualization of large variation in gene expression across samples or present in most samples, and these genes could be used for unsupervised clustering so that clustering results are not affected by the noise from absent or non-changed genes.

Thus, while, K-means clustering may be performed on all genes, the Pearson correlation is preferably calculated based on a subset of genes and

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patients. Generally speaking the larger the threshold for accepting a deviation or change from the geometric mean, the smaller the number of genes that is selected by this filtering procedure. Different cut-off or threshold values were used to prepare lists with different numbers of genes. The higher the number of genes selected and included on such lists, the more noise is generally encountered within the dataset, because there will be a relatively large contribution of non-leukemia pathway related genes in such lists. The filtering and selection procedure is preferably optimized such that the analysis is performed on as much genes as possible, while minimizing the noise.

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All genes with changed expression values higher than or equal to 1.5 times the log(2) transformed expression values and genes with changed expression values lower than or equal to -1.5 times the log(2) transformed expression values are selected for hierarchical clustering.

The subset of genes showing a markedly higher or lower expression than the geometric mean may for instance be a value that is more than 1.5 times the geometric mean value, preferably more than 2 times the geometric mean value, even more preferably more than 3 times the geometric mean value. Likewise, a markedly lower expression than the geometric mean expression level may for instance be a value that is less than 0.8 times the geometric mean value, preferably less than 0.6 times the geometric mean value, more preferably less than 0.3 times the geometric mean value. The same selection of genes that is used for the hierarchical clustering, is used for clustering of the patients by Pearson correlation coefficient analysis.

Gene expression profiling has previously been demonstrated to be useful in distinguishing myeloid from lymphoid malignancies as well as subclasses within these diseases (Alizadeh et al., 2000; Armstrong et al., 2002; Debernardi et al., 2003; Ross et al., 2003; Yeoh; Schoch et al., 2002; Golub et al., 1999), but it was hitherto unknown whether suitable distinctions on the basis of gene expression alone could be made between various types of AML,

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let alone whether such distinctions could bear any relevance to prognosis of the disease.

The present invention now provides several methods to accurately identify known as well as newly discovered diagnostically, prognostically and therapeutically relevant subgroups of acute myeloid leukemia (AML), herein below also addressed as AML classes, as well as methods that can predict which approaches in treatment are likely to be effective. The basis of these methods resides in the measurement of (AML-specific) gene expression in AML-affected subjects. The methods and compositions of the invention thus provide tools useful in choosing a therapy for AML patients, including methods for assigning an AML patient to an AML class or AML cluster, methods of choosing a therapy for an AML patient, methods of determining the efficacy of a therapy in an AML patient, and methods of determining the prognosis for an AML patient.

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The methods of the invention comprise in various aspects the steps of establishing a gene expression profile of subject samples, for instance of reference subjects affected by AML or of a subject diagnosed or classified for AML. The expression profiles of the present invention are generated from samples from subjects affected by AML, including subjects having AML, subjects suspected of having AML, subjects having a propensity to develop AML, or subjects who have previously had AML, or subjects undergoing therapy for AML. The samples from the subject used to generate the expression profiles of the present invention can be derived from a variety of sources including, but not limited to, single cells, a collection of cells, tissue, cell culture, bone marrow, blood, or other bodily fluids. The tissue or cell source may include a tissue biopsy sample, a cell sorted population, cell culture, or a single cell. Sources for the sample of the present invention include cells from peripheral blood or bone marrow, such as blast cells from peripheral blood or bone marrow.

In selecting a sample, the percentage of the sample that constitutes cells having differential gene expression in AML classes should be considered. Samples may comprise at least 20%, at least 30%, at least 40%, at least 50%, at least 55%, at least 60°/", at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% cells having differential expression in AML classes, with a preference for samples having a high percentage of such cells. In some embodiments, these cells are blast cells, such as leukernic cells. The percentage of a sample that constitutes blast cells may be determined by methods well known in the art; see, for example, the methods described in WO 03/083140.

"Gene expression profiling" or "expression profiling" is used herein in its art-recognised meaning and refers to a method for measuring the transcriptional state (mRNA) or the translational state (protein) of a plurality of genes in a cell. Depending on the method used, such measurements may involve the genome-wide assessment of gene expression, but also the measurement of the expression level of selected genes, resulting in the establishment of a "gene expression profile" or "expression profile", which terms are used in that meaning hereinbelow. As used herein, an "expression profile" comprises one or more values corresponding to a measurement of the relative abundance of a gene expression product. Such values may include measurements of RNA levels or protein abundance. Thus, the expression profile can comprise values representing the measurement of the transcriptional state or the translational state of the gene. In relation thereto, reference is made to U.S. Pat. Nos. 6,040,138, 5,800,992, 6,020135, 6,344,316, and 6,033,860.

The transcriptional state of a sample includes the identities and relative abundance of the RNA species, especially mRNAs present in the sample. Preferably, a substantial fraction of all constituent RNA species in the sample are measured, but at least a sufficient fraction to characterize the transcriptional state of the sample is measured. The transcriptional state can

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be conveniently determined by measuring transcript abundance by any of several existing gene expression technologies.

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Translational state includes the identities and relative abundance of the constituent protein species in the sample. As is known to those of skill in the art, the transcriptional state and translational state are related.

Each value in the expression profiles as determined and embodied in the present invention is a measurement representing the absolute or the relative expression level of a differentially-expressed gene. The expression levels of these genes may be determined by any method known in the art for assessing the expression level of an RNA or protein molecule in a sample. For example, expression levels of RNA may be monitored using a membrane blot (such as used in hybridization analysis such as Northern, Southern, dot, and the like), or microwells, sample tubes, gels, beads or fibers (or any solid support comprising bound nucleic acids). See U.S. Patent Nos. 5,770,722, 5,874,219, 5,744,305, 5,677,195 and 5,445,934, to which explicit reference is made. The gene expression monitoring system may also comprise nucleic acid probes in solution.

In one embodiment of the invention, microarrays are used to measure the values to be included in the expression profiles. Microarrays are particularly well suited for this purpose because of the reproducibility between different experiments. DNA microarrays provide one method for the simultaneous measurement of the expression levels of large numbers of genes. Each array consists of a reproducible pattern of capture probes attached to a solid support. Labeled RNA or DNA is hybridized to complementary probes on the array and then detected by laser scanning. Hybridization intensities for each probe on the array are determined and converted to a quantitative value representing relative gene expression levels. See, the Experimental section. See also, U.S. Pat. Nos. 6,040,138, 5,800,992 and 6,020,135, 6,033,860, and 6,344,316, to which explicit reference is made. High-density oligonucleotide

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arrays are particularly useful for determining the gene expression profile for a large number of RNA's in a sample.

In one approach, total mRNA isolated from the sample is converted to labeled cRNA and then hybridized to an oligonucleotide array. Each sample is hybridized to a separate array. Relative transcript levels are calculated by reference to appropriate controls present on the array and in the sample. See, for example, the Experimental section.

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In another embodiment, the values in the expression profile are obtained by measuring the abundance of the protein products of the differentially-expressed genes. The abundance of these protein products can be determined, for example, using antibodies specific for the protein products of the differentially-expressed genes. The term "antibody" as used herein refers to an immunoglobulin molecule or immunologically active portion thereof, i.e., an antigen-binding portion. Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')2 fragments which can be generated by treating the antibody with an enzyme such as pepsin. The antibody can be a polyclonal, monoclonal, recombinant, e.g., a chimeric or humanized, fully human, non-human, e.g., murine, or single chain antibody. In a preferred embodiment it has effector function and can fix complement. The antibody can be coupled to a toxin or imaging agent. A full-length protein product from a differentially-expressed gene, or an antigenic peptide fragment of the protein product can be used as an immunogen. Preferred epitopes encompassed by the antigenic peptide are regions of the protein product of the differentially-expressed gene that are located on the surface of the protein, e.g., hydrophilic regions, as well as regions with high antigenicity. The antibody can be used to detect the protein product of the differentiallyexpressed gene in order to evaluate the abundance and pattern of expression of the protein. These antibodies can also be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given therapy. Detection can be facilitated

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by coupling (i.e., physically linking) the antibody to a detectable substance (i.e., antibody labeling). Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, (3-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ¹²⁵I, ¹³¹I, ³⁵S or ³H.

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Once the values comprised in the subject expression profile and the reference expression profile or expression profiles are established, the subject profile is compared to the reference profile to determine whether the subject expression profile is sufficiently similar to the reference profile. Alternatively, the subject expression profile is compared to a plurality of reference expression profiles to select the reference expression profile that is most similar to the subject expression profile. Any method known in the art for comparing two or more data sets to detect similarity between them may be used to compare the subject expression profile to the reference expression profiles. In some embodiments, the subject expression profile and the reference profile are compared using a supervised learning algorithm such as the support vector machine (SVM) algorithm, prediction by collective likelihood of emerging patterns (PCL) algorithm, the k-nearest neighbour algorithm, or the Artificial Neural Network algorithm. To determine whether a subject expression profile shows "statistically significant similarity" or "sufficient similarity" to a reference profile, statistical tests may be performed to determine whether the similarity between the subject expression profile and the reference expression

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profile is likely to have been achieved by a random event. Any statistical test that can calculate the likelihood that the similarity between the subject expression profile and the reference profile results from a random event can be used. The accuracy of assigning a subject to an AML class based on similarity between differentially-expressed genes is affected largely by the heterogeneity within the patient population, as is reflected by the deviation from the geometric mean. Therefore, when more accurate diagnoses are required, the stringency in evaluating the similarity between the subject and the reference profile should be increased by changing the numerical query.

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The method used for comparing a subject expression profile to one or more reference profiles is preferably carried out by re-running the subsequent analyses in a (n+1) modus by performing clustering methods as described herein. Also, in order to identify the AML class reference profile that is most similar to the subject expression profile, as performed in the methods for establishing the AML class of an AML affected subject, i.e. by diagnosing AML in a subject or by classifying the AML in a subject, profiles are clustered according to similarity and it is determined whether the subject profile corresponds to a known class of reference profiles. In assigning a subject AML to a specific AML class for instance, this method is used wherein the clustered position of the subject profile, obtained after performing the clustering analysis of the present invention, is compared to any known AML class. If the clustered position of the subject profile is within a cluster of reference profiles, i.e. forms a cluster therewith after performing the similarity clustering method, it is said that the AML of the subject corresponds to the AML class of reference profiles. If a subject profile is not within a cluster of reference profiles, i.e. does not form a cluster therewith after performing the similarity clustering method, then a new AML class may be assigned to that subject profile, one of such classes being subjects not having AML.

In some embodiments of the present invention, the expression profiles comprise values representing the expression levels of genes that are

differentially-expressed in AML classes. The term "differentially-expressed" as used herein means that the measured expression level of a particular gene in the expression profile of one subject differs at least n-fold from the geometric mean calculated from all patient profiles. The expression level may be also be up-regulated or down-regulated in a sample from a subject having a particular form of AML in comparison with a sample from a subject having a different form of AML. For example, in one embodiment, the differentially-expressed genes of the present invention may be expressed at different levels in different AML classes. Examples of genes that are differentially-expressed in the various AML classes are shown in Tables 1 and 2.

It should be noted that many genes will occur, of which the measured expression level differs at least n-fold from the geometric mean expression level for that gene of all reference profiles. This may for instance be due to the different physiological state of the measured cells, to biological variation or to the present of other diseased states. Therefore, the presence of a differentially-expressed gene is not necessarily informative for determining the presence of different AML classes, nor is every differentially-expressed gene suitable for performing diagnostic tests. Moreover, a cluster-specific differential gene expression, as defined herein, is most likely to be informative only in a test among subjects having AML. Therefore, a diagnostic test performed by using cluster-specific gene detection should preferably be performed on a subject in which the presence of AML is confirmed. This confirmation may for instance be obtained by performing the method for classifying an AML in an AML-affected subject according to the present invention, or by any other test.

The present invention provides groups of genes that are differentially-expressed in diagnostic AML samples of patients in different AML classes. Some of these genes were identified based on gene expression levels for 13,000 probes in 286 AML samples. Values representing the expression levels of the nucleic acid molecules detected by the probes were

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analyzed as described in the Experimental section using Omniviz, SAM and PAM analysis tools. Omniviz software was used to perform all clustering steps such as K-means, Hierarchical and Pearson correlation tests. SAM was used specifically to identify the genes underlying the clinically relevant groups identified in the Pearson correlation analysis. PAM is used to decide the minimum number of genes necessary to diagnose all individual patients within the given groups of the Pearson correlation.

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In short, expression profiling was carried out on AML blasts from 286 de novo AML patients. Unsupervised clustering was used to identify novel (sub)groups within the Pearson correlation following the hierarchical clustering. The Pearson correlation test resulted in the identification of 16 groups or classes of AML patients with distinct molecular signatures. The hierarchical clustering and Pearson correlation allow the detection of the genetic heterogeneity (16 clusters). This may provide for a mechanistic signature of AML. After running the SAM and PAM analysis the diagnostic gene-signatures (incl. cluster-specific genes) were obtained.

While several of the molecularly assigned classes correspond to the well-defined AML subgroups with favourable cytogenetics, such as the well recognised genetic lesions AML1/ETO, $PML/RAR\alpha$ and $CBF\beta/MYH11$, we identified several additional distinct classes of patients that were not identified as distinct classes of AML before. For instance, new identified AML clusters comprised genetic lesions such as $CEBP\alpha$ mutations, or FLT3 ITD mutations, or 11q23 aberrations, indicating that these cytogenetic markers alone are not sufficient to determine the prognosis of an AML patient or the most optimal intervention strategy (drug treatment).

Whereas the well-defined AML subgroups AML1/ETO, $PML/RAR\alpha$ and $CBF\beta/MYH11$, could be identified based on measurement of the expression level of only one or two genes in a cell sample, many of the newly discovered AML classes were defined on the basis of differential expression of a plurality of genes. Genes that define an AML class are hereinafter also

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termed cluster-specific genes or signature genes. Prediction Analysis of Microarrays (PAM) was applied to determine the minimal gene sets that predict these prognostically important clusters with high accuracy. In one of the novel clusters half of the AML patients had unfavourable markers, such as elevated expression of EVI1 and/or loss of chromosome 7(q). Interestingly, more then 90 percent of patients in this cluster (cluster no. 10, see Example) responded poorly to therapy. The fact that a distinct gene expression signature defines this class of AML patients, suggests the existence of a currently unknown gene- or pathway defect that corresponds with poor treatment outcome.

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The present invention thus provides a method of classifying AML. Using this method, a total of 286 AML samples analysed on a DNA microarray consisting of 22283 probe sets, representing approximately 13,000 genes could be classified into at least 16 distinct clusters. These 16 distinct clusters of AML patients were assigned on the basis of strong correlation between their individual differential expression profiles for 2856 probe sets (Table 1; Figure 1). The methods used to analyze the expression level values to identify differentially-expressed genes were employed such that optimal results in clustering, i.e. unsupervised ordering, were obtained. This then resulting in the definition of the 16 clusters of reference profiles based on molecular signature. The genes that defined the position or clustering of these 16 individual clusters could be determined and the minimal sets of genes required to accurately predict the prognostically important AML classes corresponding to these clusters could be derived. It should be understood that the method for classifying AML according to the present invention may result in a distinct clustering pattern and therefore in a different classification scheme when other (numbers of) subjects are used as reference, or when other types of oligonucleotide microarrays for establishing gene expression profiles are used.

The present invention thus provides a comprehensive classification of AML covering various previously identified genetically defined classes.

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Further analysis of classes by prediction analysis of microarrays (PAM) to determine the minimum number of genes that defined or predicted these prognostically important classes resulted in the establishment of cluster-specific genes or signature genes. The presence of distinct gene expression profiles defining the novel classes suggests the presence of yet unknown common gene defects or pathway defects among AML cases in those classes. Several classes could be distinguished on the basis of the expression level of a single gene, whereas others could only be distinguished on the basis of 20 or more differentially-expressed genes (Table 3).

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The methods of the present invention comprise in some aspects the step of defining cluster-specific genes by selecting those genes of which the expression level characterizes the clustered position of the corresponding AML class among the various AML classes within a classification scheme of the present invention. Such cluster-specific genes are selected preferably on the basis of PAM analysis. This method of selection comprises the following.

PAM, or partition round medoids, is one of the k-medoids methods. Different from usual k-means approach, it also accepts a dissimilarity matrix, and it is more robust because it minimizes a sum of dissimilarities instead of a sum of squared Euclidean distances. The PAM-algorithm is based on the search for 'k' representative objects or medoids among the observations of the dataset, which should represent the structure of the data. After finding a set of 'k' medoids, 'k' clusters are constructed by assigning each observation to the nearest medoid. The goal is to find 'k' representative objects which minimize the sum of the dissimilarities of the observations to their closest representative object. The distance metric to be used for calculating dissimilarities between observations are "euclidean" and "manhattan". Euclidean distances are root sum-of-squares of differences, and manhattan distances are the sum of absolute differences. PAM calculates how many genes are necessary to identify all members (patients) belonging to a certain cluster.

The methods of the present invention comprise in some aspects the step of establishing whether the level of expression of cluster-specific genes in a subject shares sufficient similarity to the level of expression that is characteristic for an individual AML class. This step is necessary in determining the presence of that particular AML class in a subject under investigation, in which case the expression of that gene is used as a disease marker. Whether the level of expression of cluster-specific genes in a subject shares sufficient similarity to the level of expression of that particular gene in an individual AML class may for instance be determined by setting a threshold value.

The present invention also reveals genes with a high differential level of expression in specific AML classes compared the geometric mean of all reference subjects. These highly differentially-expressed genes are selected from the genes shown in Table 2. These genes and their expression products are useful as markers to detect the presence of AML in a patient. Antibodies or other reagents or tools may be used to detect the presence of these markers of AML.

The present invention also reveals gene expression profiles comprising values representing the expression levels of genes in the various identified AML classes. In a preferred embodiment, these expression profiles comprise the values representing the differential expression levels. Thus, in one embodiment the expression profiles of the invention comprise one or more values representing the expression level of a gene having differential expression in a defined AML class. Each expression profile contains a sufficient number of values such that the profile can be used to distinguish one AML class from another. In some embodiments, the expression profiles comprise only one value. For example, it can be determined whether a subject affected by AML is in the AML class defined by cluster # 9 (inv(16)) based only on the expression level of MYH11 201497_x_at (see Tables 2 and 31). Similarly, it can be determined whether a subject affected by AML is in the

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AML class defined by cluster # 12 (t(15,17)) based only on the expression level of the cDNA of 2 genes FGF13 205110_s_at and HGF 210997_at and 210998 s at (see Tables 2 and 34). In this case, the expression profile comprises two values corresponding to two differentially-expressed genes. In other embodiments, the expression profile comprises more than one or two values corresponding to a differentially-expressed gene, for example at least 3 values, at least 4 values, at least 5 values, at least 6 values, at least 7 values, at least 8 values, at least 9 values, at least 10 values, at least 11 values, at least 12 values, at least 13 values, at least 14 values, at least 15 values, at least 16 values, at least 17 values, at least 18 values, at least 19 values, at least 20 values, at least 22 values, at least 25 values, at least 27 values, at least 30 values, at least 35 values, at least 40 values, at least 45 values, at least 50 values, at least 75 values, at least 100 values, at least 125 values, at least 150 values, at least 175 values, at least 200 values, at least 250 values, at least 300 values, at least 400 values, at least 500 values, at least 600 values, at least 700 values, at least 800 values, at least 900 values, at least 1000 values, at least 1200 values, at least 1500 values, or at least 2000 or more values.

It is recognized that the diagnostic accuracy of assigning a subject to an AML class will vary based on the number of values contained in the expression profile. Generally, the number of values contained in the expression profile is selected such that the diagnostic accuracy is at least 85%, at least 87%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, as calculated using methods described elsewhere herein, with an obvious preference for higher percentages of diagnostic accuracy.

It is recognized that the diagnostic accuracy of assigning a subject to an AML class will vary based on the strength of the correlation between the expression levels of the differentially-expressed genes within that specific AML class. When the values in the expression profiles represent the expression levels of genes whose expression is strongly correlated with that specific AML

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class, it may be possible to use fewer number of values (genes) in the expression profile and still obtain an acceptable level of diagnostic or prognostic accuracy.

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The strength of the correlation between the expression level of a differentially-expressed gene and a specific AML class may be determined by a statistical test of significance. For example, the chi square test used to select genes in some embodiments of the present invention assigns a chi square value to each differentially-expressed gene, indicating the strength of the correlation of the expression of that gene to a specific AML class. Similarly, the T-statistics metric and the Wilkins' metric both provide a value or score indicative of the strength of the correlation between the expression of the gene and its specific AML class. These scores may be used to select the genes of which the expression levels have the greatest correlation with a particular AML class to increase the diagnostic or prognostic accuracy of the methods of the invention, or in order to reduce the number of values contained in the expression profile while maintaining the diagnostic or prognostic accuracy of the expression profile. Preferably, a database is kept wherein the expression profiles of reference subjects are collected and to which database new profiles can be added and clustered with the already existing profiles such as to provide the clustered position of said new profile among the already present reference profiles. Furthermore, the addition of new profiles to the database will improve the diagnostic and prognostic accuracy of the methods of the invention. Preferably, in a method of the present invention SAM or PAM analysis tools are used to determine the strength of such correlations.

The methods of the invention comprise the steps of providing an expression profile from a sample from a subject affected by AML and comparing this subject expression profile to one or more reference profiles that are associated with a particular AML class, a class with a known prognosis, or a class with a favourable response to therapy. By identifying the AML class reference profile that is most similar to the subject expression profile, e.g.

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when their clustered positions fall together, the subject can be assigned to an AML class. The AML class assigned is that with which the reference profile(s) are associated. Similarly, the prognosis of a subject affected by AML can be predicted by determining whether the expression profile from the subject is sufficiently similar to a reference profile associated with an established prognosis, such as a good prognosis or a bad prognosis. Whenever a subject's expression profile can be assigned to an established AML class, a preferred intervention strategy, or therapeutic treatment can then be proposed for said subject, and said subject can be treated according to said assigned strategy. As a result, treatment of a subject with AML can be optimized according to the specific class of AML with which the subject is affected. For instance, the AML class belonging to cluster # 12, characterized by the presence of t(15,17), may be treated with retinoic acid. Within one class or cluster, further division may be made according to responders and non-responders to treatment or therapy. Such divisions may provide for further detailed characterisation of AML subjects. In another embodiment, the subject expression profile is from a subject affected by AML who is undergoing a therapy to treat the AML. The subject expression profile is compared to one or more reference expression profiles to monitor the efficacy of the therapy.

In some embodiments, the assignment of a subject affected by AML to an AML class is used in a method of choosing a therapy for the subject affected by AML. A therapy, as used herein, refers to a course of treatment intended to reduce or eliminate the affects or symptoms of a disease, in this case AML. A therapy regime will typically comprise, but is not limited to, a prescribed dosage of one or more drugs or hematopoietic stem cell transplantation. Therapies, ideally, will be beneficial and reduce the disease state but in many instances the effect of a therapy will have non-desirable effects as well.

In one aspect, the present invention provides a method of determining the prognosis for an AML affected subject, said method

comprising the steps of providing a classification scheme for AML by producing such a scheme according to a method of the invention and determining the prognosis for each AML class in said scheme based on clinical records for the AML subjects comprised in said class. In order to predict the progression of the disease in a subject, one has to rely on clinical records. The present invention provides for the assignment of the various clinical data recorded with reference subjects affected by AML to the various AML classes as defined herein. This assignment preferably occurs in a database. This has the advantage that once a new subject is identified as belonging to a particular AML class, either by performing a specific AML diagnostic method of the invention using the cluster-specific genes as disease markers or by performing a method of classifying an AML in an AML affected subject according to the invention, then the prognosis that is assigned to that class may be assigned to that subject.

The present invention provides compositions that are useful in determining the gene expression profile for a subject affected by AML and selecting a reference profile that is similar to the subject expression profile. These compositions include arrays comprising a substrate having capture probes that can bind specifically to nucleic acid molecules that are differentially-expressed in AML classes. Also provided is a computer-readable medium having digitally encoded reference profiles useful in the methods of the claimed invention.

The present invention provides arrays comprising capture probes for detection of polynucleotides (transcriptional state) or for detection of proteins (translational state) in order to detect differentially-expressed genes of the invention. By "array" is intended a solid support or substrate with peptide or nucleic acid probes attached to said support or substrate. Arrays typically comprise a plurality of different nucleic acid or peptide capture probes that are coupled to a surface of a substrate in different, known locations. These arrays, also described as "microarrays" or colloquially "chips" have been generally

described in the art, and reference is made U.S. Patent. Nos. 5,143,854, 5,445,934, 5,744,305, 5,677,195, 6,040,193, 5,424,186,6,329,143, and 6,309,831 and Fodor et al. (1991) Science 251:767-77. These arrays may generally be produced using mechanical synthesis methods or light directed synthesis methods which incorporate a combination of photolithographic methods and solid phase synthesis methods. Typically, "oligonucleotide microarrays" will be used for determining the transcriptional state, whereas "peptide microarrays" will be used for determining the translational state of a cell.

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"Nucleic acid" or "oligonucleotide" or "polynucleotide" or grammatical equivalents used herein means at least two nucleotides 10 covalently linked together. Oligonucleotides are typically from about 5, 6, 7, 8, 9, 10, 12, 15, 25, 30, 40, 50 or more nucleotides in length, up to about 100 nucleotides in length. Nucleic acids and polynucleotides are a polymers of any length, including longer lengths, e.g., 200, 300, 500, 1000, 2000, 3000, 5000, 7000, 10,000, etc. A nucleic acid of the present invention will generally contain 15 phosphodiester bonds, although in some cases, nucleic acid analogs are included that may have alternate backbones, comprising, e.g., phosphoramidate, phosphorothioate, phosphorodithioate, or Omethylphophoroamidite linkages (see Eckstein, Oligonucleotides and Analogues: A Practical Approach, Oxford University Press); and peptide 20 nucleic acid backbones and linkages. Other analog nucleic acids include those with positive backbones; non-ionic backbones, and non-ribose backbones, including those described in U.S. Pat. Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, Carbo hydrate Modifications in Antisense Research, Sanghui & Cook, eds. Nucleic acids containing one or 25 more carbocyclic sugars are also included within one definition of nucleic acids. Modifications of the ribose-phosphate backbone may be done for a variety of reasons, e.g. to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip. Mixtures of naturally occurring nucleic acids and analogs can be made; alternatively, mixtures of 30

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different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

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Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially nonionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature (T_m) for mismatched versus perfectly matched basepairs. DNA and RNA typically exhibit a 2-4 °C drop in T_m for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to 7-9°C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand also defines the sequence of the complementary strand; thus the sequences described herein also provide the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc.

"Transcript" typically refers to a naturally occurring RNA, e.g., a pre-mRNA, hnRNA, or mRNA. As used herein, the term "nucleoside" includes nucleotides and nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures. Thus, e.g. the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

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As used herein a "nucleic acid probe or oligonucleotide" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (i.e., A, G, C, or T) or modified bases (7-deazaguanosine, inosine, etc.). In addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not functionally interfere with hybridization. Thus, e.g., probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. The probes are preferably directly labeled such as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind or with enzymatic labels. By assaying for the hybridization of the probe to its target nucleic acid sequence, one can detect the presence or absence of the select sequence or subsequence. Diagnosis or prognosis may be based at the genomic level, or at the level of RNA or protein expression.

The skilled person is capable of designing oligonucleotide probes that can be used in diagnostic methods of the present invention. Preferably, such probes are immobilised on a solid surface as to form an oligonucleotide microarray of the invention. The oligonucleotide probes useful in methods of the present invention are capable of hybridizing under stringent conditions to AML-associated nucleic acids, such as to one or more of the genes selected from Table 1, preferably to one or more of the genes selected from Table 2, more preferably to one or more of the genes selected from Table 3.

Techniques for the synthesis of arrays using mechanical synthesis methods are described in, e.g., U.S. Patent No. 5,384,261, to which reference is made herein. Although a planar array surface is preferred, the array may be

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fabricated on a surface of virtually any shape or even a multiplicity of surfaces. Arrays may be peptides or nucleic acids on beads, gels, polymeric surfaces, fibers such as fiber optics, glass or any other appropriate substrate, for the purpose of which reference is made to U.S. Pat. Nos. 5,770,358, 5,789, 162, 5,708,153, 6,040,193 and 5,800,992. Arrays may be packaged in such a manner as to allow for diagnostics or other manipulation of an all-inclusive device. Reference is for example made to U.S. Pat. Nos. 5,856,174 and 5,922,591.

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The arrays provided by the present invention comprise capture probes that can specifically bind a nucleic acid molecule that is differentially-expressed in AML classes. These arrays can be used to measure the expression levels of nucleic acid molecules to thereby create an expression profile for use in methods of determining the diagnosis and prognosis for AML patients, and for monitoring the efficacy of a therapy in these patients as described elsewhere herein.

In some embodiments, each capture probe in the array detects a nucleic acid molecule selected from the nucleic acid molecules designated in Tables 1 and 2. The designated nucleic acid molecules include those differentially-expressed in AML classes selected from cluster #1-cluster #16 as depicted in figure 1.

The arrays of the invention comprise a substrate having a plurality of addresses, where each address has a capture probe that can specifically bind a target nucleic acid molecule. The number of addresses on the substrate varies with the purpose for which the array is intended. The arrays may be low-density arrays or high-density arrays and may contain 4 or more, 8 or more, 12 or more, 16 or more, 20 or more, 24 or more, 32 or more, 48 or more, 64 or more, 72 or more 80 or more, 96, or more addresses, or 192 or more, 288 or more, 384 or more, 768 or more, 1536 or more, 3072 or more, 6144 or more, 9216 or more, 12288 or more, 15360 or more, or 18432 or more addresses. In some embodiments, the substrate has no more than 12, 24, 48, 96, or 192, or

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384 addresses, no more than 500, 600, 700, 800, or 900 addresses, or no more than 1000, 1200, 1600, 2400, or 3600 addresses.

The invention also provides a computer-readable medium comprising one or more digitally encoded expression profiles, where each profile has one or more values representing the expression of a gene that is differentially-expressed in an AML class. The preparation and use of such profiles is well within the reach of the skilled person (see e.g. WO 03/083140). In some embodiments, the digitally-encoded expression profiles are comprised in a database. See, for example, U.S. Patent No. 6,308,170.

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The present invention also provides kits useful for diagnosing, treating, and monitoring the disease state in subjects affected by AML. These kits comprise an array and a computer readable medium. The array comprises a substrate having addresses, where each address has a capture probe that can specifically bind a nucleic acid molecule (by using an oligonucleotide array) or a peptide (by using a peptide array) that is differentially-expressed in at least one AML class. The results are converted into a computer-readable medium that has digitally-encoded expression profiles containing values representing the expression level of a nucleic acid molecule detected by the array.

By using the array described above, the amounts of various kinds of nucleic acid molecules contained in a nucleic acid sample can be simultaneously determined. In addition, there is an advantage such that the determination can be carried out even with a small amount of the nucleic acid sample. For instance, mRNA in the sample is labeled, or labeled cDNA is prepared by using mRNA as a template, and the labeled mRNA or cDNA is subjected to hybridization with the array, so that mRNAs being expressed in the sample are simultaneously detected, whereby their expression levels can be determined.

Genes each of which expression is altered due to AML can be found by determining expression levels of various genes in the AML affected cells

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and classified into certain types as described above and comparing the expression levels with the expression level in a control tissue.

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The method for determining the expression levels of genes is not particularly limited, and any of techniques for confirming alterations of the gene expressions mentioned above can be suitably used. Among all, the method using the array is especially preferable because the expressions of a large number of genes can be simultaneously determined. Suitable arrays are commercially available, e.g., from Affymetrix.

For instance, mRNA is prepared from blast cells, and then reverse transcription is carried out with the resulting mRNA as a template. During this process, labeled cDNA can be obtained by using, for instance, any suitable labeled primers or labeled nucleotides.

As to the labeling substance used for labeling, there can be used substances such as radioisotopes, fluorescent substances, chemiluminescent substances and substances with fluophor, and the like. For instance, the fluorescent substance includes Cy2, FluorX, Cy3, Cy3.5, Cy5, Cy5.5, Cy7, fluorescein isothiocyanate (FITC), Texas Red, Rhodamine and the like. In addition, it is desired that samples to be tested (cancer samples to be tested in the present selection method) and a sample to be used as a control are each labeled with different fluorescent substances, using two or more fluorescent substances, from the viewpoint of enabling simultaneous detection. Here, labeling of the samples is carried out by labeling mRNA in the samples, cDNA derived from the mRNA, or nucleic acids produced by transcription or amplification from cDNA.

Next, the hybridization is carried out between the above-mentioned labeled cDNA and the array to which a nucleic acid corresponding to a suitable gene or its fragment is immobilized. The hybridization may be performed according to any known processes under conditions that are appropriate for the array and the labeled cDNA to be used. For instance, the hybridization can

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be performed under the conditions described in Molecular Cloning, A laboratory manual, 2nd ed., 9.52-9.55 (1989).

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The hybridization between the nucleic acids derived from the samples and the array is carried out, under the above-mentioned hybridization conditions. When much time is needed for the time period required for procedures from the collection of samples to the determination of expression levels of genes, the degradation of mRNA may take place due to actions of ribonuclease. In order to determine the difference in the gene expressions in the samples to be tested (i.e., cell or tissue samples of AML patients) and the gene expressions in a control sample, it is preferable that the mRNA levels in both of these samples are adjusted using a standard gene with relatively little alterations in expressions.

Thereafter, by comparing the hybridization results of the samples to be tested with those of the control sample, genes exhibiting differential expression levels in both samples can be detected. Concretely, a signal which is appropriate depending upon the method of labeling used is detected for the array which is subjected to hybridization with the nucleic acid sample labeled by the method as described above, whereby the expression levels in the samples to be tested can be compared with the expression level in the control sample for each of the genes on the array.

The genes thus obtained which have a significant difference in signal intensities are genes each of which expression is altered specifically for certain AML classes.

The present invention also provides a computer-readable medium comprising a plurality of digitally-encoded expression profiles wherein each profile of the plurality has a plurality of values, each value representing the expression of a gene that is differentially-expressed in at least one AML class. The invention also provides for the storage and retrieval of a collection of data relating to AML specific gene expression data of the present invention, including sequences and expression levels in a computer data storage

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apparatus, which can include magnetic disks, optical disks, magneto-optical disks, DRAM, SRAM, SGRAM, SDRAM, RDRAM, DDR RAM, magnetic bubble memory devices, and other data storage devices, including CPU registers and on-CPU data storage arrays. Typically, the data records are stored as a bit pattern in an array of magnetic domains on a magnetizable medium or as an array of charge states or transistor gate states, such as an array of cells in a DRAM device (e.g., each cell comprised of a transistor and a charge storage area, which may be on the transistor).

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For use in diagnostic, research, and therapeutic applications suggested above, kits are also provided by the invention. In the diagnostic and research applications such kits may include any or all of the following: assay reagents, buffers, AML class-specific nucleic acids or antibodies, hybridization probes and/or primers, antisense polynucleotides, ribozymes, dominant negative AML polypeptides or polynucleotides, small molecules inhibitors of AML-associated sequences, arrays, antibodies, Fab fragments, capture peptides etc. In addition, the kits may include instructional materials containing directions (i.e., protocols) for the practice of the methods of this invention. While the instructional materials typically comprise written or printed materials, they are not limited to such. Any medium capable of storing such instructions and communicating them to an end user is contemplated by this invention. Such media include, but are not limited to electronic storage media (e.g., magnetic discs, tapes, cartridges, chips), optical media (e.g., CD ROM), and the like. Such media may include addresses to internet sites that provide such instructional materials. One such internet site may provide a database of AML reference expression profiles useful for performing similarity clustering of a newly determine subject expression profiles with a large set of reference profiles of AML subjects comprised in said database. Preferably the database includes clinically relevant data such as patient prognosis, successful methods of treatment and cytogenetic characteristics for the various AML classes in the database.

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The invention encompasses for instance kits comprising an array of the invention and a computer-readable medium having digitally-encoded reference profiles with values representing the expression of nucleic acid molecules detected by the arrays. These kits are useful for assigning a subject affected by AML to an AML class and for diagnosing AML in a subject.

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The present invention also provides for kits for screening for modulators of AML-associated sequences. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise one or more of the following materials: an AML-associated polypeptide or polynucleotide, reaction tubes, and instructions for testing AML-associated activity. Optionally the kit may comprise an array for detecting AML-associated genes, specifically cluster-defining genes according to the invention. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of the user.

Diagnosis would typically involve evaluation of a plurality of genes or products. The genes will be selected based on correlations with important parameters in disease which may be identified in historical or outcome data.

In a preferred embodiment a kit-of-parts according to the invention comprises an oligonucleotide microarray according to the invention and means for comparing a gene expression profile determined by using said microarray with a database of AML reference expression profiles. The present invention also comprises kits of parts suitable for performing a method of the invention as well as the use of the various products of the invention, including databases, microarrays, oligonucleotide probes and classification schemes in diagnostic or prognostic methods of the invention.

The methods and compositions of the invention may be used to screen test compounds to identify therapeutic compounds useful for the treatment of AML. In one embodiment, the test compounds are screened in a sample comprising primary cells or a cell line representative of a particular

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AML class. After treatment with the test compound, the expression levels in the sample of one or more of the differentially-expressed genes of the invention are measured using methods described elsewhere herein. Values representing the expression levels of the differentially-expressed genes are used to generate a subject expression profile. This subject expression profile is then compared to a reference profile associated with the AML class represented by the sample to determine the similarity between the subject expression profile and the reference expression profile. Differences between the subject expression profile and the reference expression profile may be used to determine whether the test compound has anti-leukemogenic activity.

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The test compounds of the present invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the 'one-bead one-compound' library method; and synthetic library methods using affinity chromatography selection. The biological library approach is limited to polypeptide libraries, while the other four approaches are applicable to polypeptide, non-peptide oligomer or small molecule libraries of compounds (Lam (1997) Anticancer Drug Res. 12:145).

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in DeWitt et al. (1993) Proc. Nad. Acad. Sci. USA 90:6909; Erb et al. (1994) Proc. Natl. Acad. Sci. USA 91:11422; Zuckermann et al. (1994) J. Med. Chem. 37:2678; Cho et al. (1993) Science 261:1303; Carell et al. (1994) Angew. Chem. Int. Ed. Engl. 33:2059; Carell et al. (1994) Angew. Chem. Int. Ed. Engl. 33:2061; and in Gallop et al. (1994) J. Med. Chem. 37:1233. Libraries of compounds may be presented in solution (e.g., Houghten (1992) Biotechniques 13:412-421), or on beads (Lam (1991) Nature 354:82-84), chips (Fodor (1993) Nature 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (U.S. Patent No. 5,223,409), plasmids (Cull et al. (1992) Proc. Natl. Acad. Sci. USA 89:1865-1869) or on phage (Scott and Smith (1990) Science

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249:386-390; Devlin (1990) Science 249:404-406; Cwirla *et al.* (1990) Proc. Nad. Acad. Sci. U.S.A. 97:6378-6382; Felici (1991) J. Mol. Biol. 222:301-310).

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Candidate compounds include, for example, 1) peptides such as soluble peptides, including Ig-tailed fusion peptides and members of random peptide libraries (see, e.g., Lam et al. (1991) Nature 354:82-84; Houghten et al. (1991) Nature 354:84-86) and combinatorial chemistry-derived molecular libraries made of D- and/or L- configuration amino acids; 2) phosphopeptides (e.g., members of random and partially degenerate, directed phosphopeptide libraries, see, e.g., Songyang et al. (1993) Cell 72:767-778); 3) antibodies (e.g., polyclonal, monoclonal, humanized, anti-idiotypic, chimeric, and single chain antibodies as well as Fab, F(ab')Z, Fab expression library fragments, and epitope binding fragments of antibodies); 4) small organic and inorganic molecules (e.g., molecules obtained from combinatorial and natural product libraries; 5) zinc analogs; 6) leukotriene A4 and derivatives; 7) classical aminopeptidase inhibitors and derivatives of such inhibitors, such as bestatin and arphamenine A and B and derivatives; 8) and artificial peptide substrates and other substrates, such as those disclosed herein above and derivatives thereof.

The present invention discloses a number of genes that are differentially-expressed in AML classes. These differentially-expressed genes are shown in Tables 1 and 2. Because the expression of these genes is associated with AML risk factors, these genes may play a role in leukemogenesis. Accordingly, these genes and their gene products are potential therapeutic targets that are useful in methods of screening test compounds to identify therapeutic compounds for the treatment of AML. Genes that are common between a number of AML classes are preferred as targets for therapeutic treatment, since a broader working over the patient population can be expected. It is very likely that genes that are present in more than one AML class, as defined in the present invention, are involved in general processes underlying AML. Thus, the expression of these genes is

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likely to be associated with AML risk factors and thus play a role in leukemogenesis. Genes that are present in several classes or clusters may thus define superclusters, which superclusters may define the processes that play an important role in leukemogenesis in general, and AML in particular.

The differentially-expressed genes of the invention may be used in cell-based screening assays involving recombinant host cells expressing the differentially-expressed gene product. The recombinant host cells are then screened to identify compounds that can activate the product of the differentially-expressed gene (i.e. agonists) or inactivate the product of the differentially-expressed gene (i.e. antagonists).

Any of the leukemogenic functions mediated by the product of the differentially-expressed gene may be used as an endpoint in the screening assay for identifying therapeutic compounds for the treatment of AML. Such endpoint assays include assays for cell proliferation, assays for modulation of the cell cycle, assays for the expression of markers indicative of AML, and assays for the expression level of genes differentially-expressed in AML classes as described above. Modulators of the activity of a product of a differentially-expressed gene identified according to these drug-screening assays provided above can be used to treat a subject with AML. These methods of treatment include the steps of administering the modulators of the activity of a product of a differentially-expressed gene in a pharmaceutical composition as described herein, to a subject in need of such treatment.

The following examples are offered by way of illustration and not by way of limitation.

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EXAMPLE 1

Methods Used

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Patients and cell samples

Patients with a confirmed diagnosis of *de novo* AML were included in this study (Table 4). All patients were treated according to the HOVON (Dutch-Belgian Hematology-Oncology Co-operative group) protocols (http://www.hovon.nl). The treatment protocols have been described previously Rombouts *et al.*, 2001). Bone marrow or peripheral blood aspirations of AML patients at diagnosis (n=286) and healthy volunteers (n=5) were taken after informed consent. Blasts and mononuclear cells were purified by Ficoll-Hypaque (Nygaard, Oslo, Norway) centrifugation and cryopreserved. CD34 positive cells of healthy volunteers (n=3) were sorted using the fluorescent activated cell sorter (FACS). According to cytological analysis the AML samples contained 80-100% blast cells after thawing independent of the blast count at diagnosis.

RNA isolation and quality control

After thawing, cells were washed once with Hanks balanced salt solution. High quality total RNA was extracted by lyses with guanidinium isothiocyanate followed by cesium chloride gradient purification (Chomczynski & Sacchi, 1987). RNA concentration, quality and purity were examined using the RNA 6000 Nano assay on the Agilent 2100 Bioanalyzer (Agilent, Amstelveen, The Netherlands). None of the samples showed RNA degradation (28S/18S rRNA ratio ≥ 2) or DNA contamination.

Gene profiling and quality control

286 newly diagnosed cases of AML (Table 3) were analyzed by gene profiling using the Affymetrix U133A GeneChip. The U133A GeneChips contain 22283 probe sets representing approximately 13000 distinct genes.

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Ten microgram of total RNA was used for the production of antisense biotinylated RNA. Single-stranded cDNA and double-stranded cDNA were synthesized according to the manufactures protocol (Invitrogen Life Technologies, Breda, The Netherlands) using the T7-(dT)24-primer (Genset Corp, Paris France). In vitro transcription was performed with biotin-11-CTP and biotin-16-UTP (Perkin Elmer, Hoofddorp, The Netherlands) and the MEGAScript T7 labeling kit (Ambion, Cambridgeshire, UK). Double-stranded cDNA and cRNA were purified and fragmented with the GeneChip Sample Cleanup Module (Affymetrix, Santa Clara, CA). Biotinylated RNA was subsequently hybridized to the Affymetrix U133A GeneChip (45°C for 16 hours). Staining, washing and scanning procedures were carried out as described in the GeneChip Expression Analysis Technical Manual (Affymetrix, Santa Clara, CA). All GeneChips were visually inspected for obvious irregularities. The global method of scaling/normalization was applied and the differences between the scaling/normalization factors of all GeneChips (n=294) were less than 3-fold (0.70, SD 0.26). All additional quality metrics, i.e. percent genes present (50.6, SD 3.8), actin 3' to 5' ratio (1.24, SD 0.19) and GAPDH 3'to 5' ratio (1.05, SD 0.14) indicated high overall sample and assay quality.

20 Data normalization, analysis and visualization

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The mean intensity values of all probe sets were calculated by the global method of scaling/normalization using MAS5.0. As most genes with values below 30 are absent (83% of all absent calls), these values were classified as unreliable and set to 30. This process resulted also in the exclusion of possibly unreliable present calls (10% of all present calls). The ratios between measured intensity and geometric mean intensity were calculated for each probe set and log2 transformed to be used for further data analyses with Omniviz®, SAM® and PAM®.

 $Omniviz^{\odot}$ (Maynard, MA (version 3.6)) – Different numbers of probe sets were selected by filtering for those genes that in one or more samples

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differed at least n-fold from the geometric mean expression level of all AML patients. By using various ratios different numbers of differentially-expressed probe sets were selected for the correlation visualization tool (Table 2). For each number of selected probe sets the clustering of the AML patients in specific molecularly recognizable groups was investigated using the Correlation Visualization tool of Omniviz (Supplemental Data (Figures B to H)).

Table 5 (below) shows the evaluation of the Correlation View results on the basis of the clustering of AML patients with similar molecular abnormalities.). The few AML cases with abnormalities involving chromosome 5 were excluded. Ratio: ratio between measured intensity and geometric mean intensity by which probe sets were selected.

SAM © (version 1.21) Trustees of Leland Stanford Junior University - All supervised analyses were performed using Significance Analysis of Microarrays (SAM) (Tusher et al., 2001). The criterion to identify the top40 genes for the assigned clusters was: at least a 2-fold difference between selected cluster and the remaining AML samples and a q-value of less than 5%.

PAM © (version 1.12) Trustees of Leland Stanford Junior University
 - All supervised class prediction analyses were performed by applying
 Prediction Analysis of Microarrays (PAM) software in R (version 1.7.1)
 (Tibshirani et al., 2002).

All genes identified by the SAM and PAM methods are available as Supplemental Data (Tables A1 to P1 and Q).

RT-PCR and sequence analyses

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Reverse trancriptase - polymerase chain reactions (RT-PCR) and sequence analyses for mutations in FLT3-ITD, FLT3-TKD, N-RAS, K-RAS and $cEBP\alpha$, as well as real-time PCR for EVI1 were performed as described

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previously (van Waalwijk van Doorn-Khosrovani et al., 2003a; van Waalwijk van Doorn-Khosrovani et al., 2003b; Valk et al., 2004; Care et al., 2003).

Statistical analyses of survival

Statistical analyses were performed with Stata Statistical Software, Release 7.0 (Stata, College Station, TX). Actuarial probabilities of overall survival (OS, with failure death due to any cause) and event-free survival (EFS, with failure in case of no complete remission at day 1, at relapse or death in first CR) were estimated by the method of Kaplan and Meier.

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Results

Correlation visualization of de novo AML by gene expression

The best unsupervised ordering by applying the visualization tool of Omniviz of the AML cases in relation to different molecular markers was reached using 2856 probe sets (representing 2008 annotated genes and 146 ESTs) (Figure 1A and Table 5). Sixteen distinct groups of AML patients were assigned on the basis of strong correlation between adjacent AML patients, i.e., within one red square along the diagonal, as well as the correlation and anti-correlation between the different groups, i.e., between the red squares along the diagonal (Figure 1A and Supplemental data (Figure A)). The final Omniviz Correlation View generated with 2856 probe sets was adapted such that cytological, cytogenetic and molecular parameters could be plotted directly adjacent to the original diagonal. This resulted in a unique way of visualization of the groups of patients with high correlation and related parameters (Figure 1B).

Distinct clusters of AML t(8;21), AML inv(16) and AML t(15;17) were apparent (Figure 1B). Although these distinct clusters were readily identified with less probe sets using the correlation tool, clusters of AML patients with mutations in FLT3 or $cEBP\alpha$, or with overexpression of EVI1 were only apparent with 2856 probe sets (Table 5 and Figures 4 to 10). When

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more genes were used for the correlation visualization this compact clustering vanished (Table 5).

Unique genes characteristic for each of the 16 identified clusters were obtained by supervised analysis using SAM. The expression profiles of the top4O genes are plotted in Figure 1B alongside the Correlation View. The SAM analyses resulted in only 599 discriminating genes (Tables 23-39) since a distinct gene profile for cluster #14 could not be identified, suggesting tight overlap with genes in clusters #7 and #8.

10 AML and recurrent translocations

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#9 (Figure 1B and Supplemental Data (Table I)). Of note, 4 patients who were previously not known to harbour an inv(16) were included within this cluster. Molecular analysis and Southern blotting revealed the presence of CBFβ/MYH11 fusion gene in those cases (Figure 11). SAM analysis revealed that MYH11 was the most prominent discriminating gene for this cluster (Supplemental data (Table I1 and Figure 12). Interestingly, CBFβ anticorrelated with this cluster, suggesting that the CBFβ/MYH11 fusion protein down modulates the expression of the CBFβ allele.

 $PML/RAR\alpha$ — Cluster #12 contains all cases of acute promyelocytic leukemia (APL) with t(15;17) (Figure 1B and Supplemental Data (Table L)), including two patients previously recognized as APL with $PML/RAR\alpha$ by RT-PCR only. SAM analyses (Supplemental Data (Table L1)) revealed that genes encoding growth factors such as hepatocyte growth factor (HGF), macrophage-stimulating 1 (hepatocyte growth factor-like (MSTI)) and fibroblast growth factor 13 (FGF13) were specific for this cluster. In addition, cluster #12 could be separated into two subgroups with either high or low white blood cell count (WBC) (Supplemental data (Figure 13). This subdivision corresponds with FLT3 ITD mutation status (Figure 1B).

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AML1/ETO - All patients with a t(8;21) grouped within cluster #13 (Figure 1B and Supplemental Data (Table M)), including one patient without a t(8;21) (2496). SAM identified ETO as the most discriminative gene for this cluster (Supplemental data (Table M1 and Figure 14).

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AML with 11q23 abnormalities

AML patients with 11q23 abnormalities were intermingled within the 286 AML patients, although two subgroups were apparent, i.e., cluster #1 and cluster #16 (Figure 1B and Supplemental Data (Tables A and P)). Cluster #16 contains four cases of t(9;11) and one case of t(11;19) (5/11 cases (45%)). SAM analyses identified a strong signature with a group of genes specifically upregulated in the majority of cases in this cluster (Figure 1B and Supplemental data (Table P1)). Although seven of 14 (50%) cases within cluster #1 have chromosome 11 abnormalities as well, this subgroup appears quite heterogeneous with a less uniform signature (Figure 1B).

AML and cEBPa mutations

Interestingly, two separate clusters (#4 and #15) comprise AML patients with predominantly normal karyotypes and a high frequency of mutations in $cEBP\alpha$ (Figure 1B (Clusters #4 (8/15 cases (53%)) and #15 (5/8 cases (62%))). In cluster #4 a set of up- and down regulated genes could be defined (Supplemental data (Table D1)), which appeared to discriminate the AML cases in cluster #4 from cluster #15. The upregulated genes represent certain T-cell genes, such as the CD7 antigen (CD7) and the T cell receptor delta locus (TRD@), which are known to be expressed on immature subsets of AML as well (Lo Coco et al., 1989; Boeckx et al., 2002). All but one of the top40 genes of cluster #15 are downregulated (Supplemental data (Table O1)). Interestingly, these genes are similarly downregulated in cluster #4 (Figure 1B). The genes encoding alpha1-catenin (CTNNA1), tubulin beta-5 (TUBB5)

and Nedd4 family interacting protein 1 (*NDFIP1*) were the only genes down modulated and among the top40 in both cluster #4 and #15.

AML and EVI1 overexpression

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A separate cluster (#10) of AML was identified in which 44% (10/22 cases, Supplemental data (Table J)) showed increased expression of EVI1. Aberrant expression of EVI1 in cluster #10 correlated with chromosome 7 abnormalities (6/10 EVI1-positive cases). This complete group of patients could be discriminated based on a selection of genes, suggesting that all patients, even the EVI1 negative cases, carry abnormalities in a common pathway. Cluster #8 also contains a relatively high number of chromosome 7 aberrations (5/13 cases, Supplemental data (Table H)), but it displays a different molecular signature compared to cluster #10 (Figure 1B). This suggests that high expression of EVI1 and/or EVI1-related proteins determines the molecular profile of cluster #10. Four out of 14 cases within the heterogeneous cluster #1 also demonstrated increased EVI1 expression. These patients may cluster outside cluster #10 since their molecular signatures are most likely the result of EVI1 overexpression and an 11q23 abnormality.

20 AML with FLT3 mutations

Groups of patients with mutations in the *FLT3* receptor gene were recognized within the Correlation View (Figure 1B). In fact, clusters #2 and #6 merely consist of patients with a *FLT3* ITD. Interestingly, almost all of these patients have a normal karyotype. In addition, the *FLT3* ITD mutation status seems to divide several clusters into two groups, e.g., clusters #3, #5 and AML with t(15;17) (#12). Other individual cases of AML with *FLT3* ITD were more dispersed over the whole group of AML patients. AML patients with mutations in the tyrosine kinase domain (TKD) of *FLT3* did not cluster. Likewise patients with mutations in codons 12, 13 or 61 of the small GTPase RAS (N-

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RAS and K-RAS) do not have apparent signatures and do not aggregate in the Correlation View (Figure 1B).

Other unique AML clusters

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AML patients with normal karyotypes clustered in several subgroups within the assigned clusters (Figure 1B). In fact, the majority of patients in cluster #11 have normal karyotypes without any consistent additional abnormality. Other unique clusters, i.e., cluster #3, #5, #7, #8 and #14, were identified which could not be annotated with any known cytogenetic or molecular abnormality. Cluster #5 mainly contains AML patients that belong to the French-American-British (FAB) classification M4 or M5 subtypes (Figure 1B), suggesting that the morphology was the main determinant for classifying these cases within this subgroup. Clusters #3, #7, #8, #11 and #14 contain AML cases, that do not belong to one FAB subtype, but can be discriminated based on distinct gene expression profiles.

Class prediction of distinct clusters in AML

All 286 AML cases were randomised and divided into a training-(n=190) and a validation set (n=96). PAM was applied on the dataset to determine the minimal number of genes to predict distinct abnormalities with prognostic value in AML¹, i.e., t(8;21), inv(16), t(15;17), 11q23 (cluster #16), EVII/monosomy 7 (cluster #10), $cEBP\alpha$ (clusters #4 and #15) (Table 3). In addition, since FLT3 ITD mutations are frequent abnormalities in AML and associated with poor outcome², the minimal set of genes to predict FLT3 ITD mutations in AML were identified.

All patients with favourable cytogenetics within the validation set were predicted with 100% accuracy and with only few genes (Table 3). As expected from the SAM analyses, *ETO* for t(8;21), *MYH11* for inv(16) and *HGF* for t(15;17) were among the most predictive genes (Supplemental Data (Table Q)). Interestingly, cluster #10 (*EVI1*/ monosomy 7) was predicted with high

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accuracy, although with a higher 10-fold cross validation error. Cluster #16 (11q23) was predicted with fairly high accuracy. Since cluster #15 (cEBP α) consists of few patients only, we combined both cEBP α clusters. These two clusters could subsequently be predicted within the validation set with fairly high accuracy. A highly predictive signature for the *FLT3* ITD cluster could not be defined by means of expression profiling within the AML patient cohort investigated.

Table 3 (below) shows the class prediction using PAM (10-fold CV error: 10-fold cross validation prediction error on training set (n=190), Error validation set: prediction error on validation set (n=96), #Probe sets: Number of probe sets used for prediction, #Genes: number of genes represented by probe sets used for prediction. For identities of the probe sets and genes see Supplemental Data (Table Q). *After randomization none of the AML patients from $cEBP\alpha$ cluster #15 were included in the validation set.

Survival analyses

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Overall survival (OS), event free survival (EFS) and relapse rate (RR) of AML patients from clusters containing >20 cases in the Correlation View, were determined, i.e., clusters #5 (M4/M5), #9 (inv(16)), #10 (EVI1/monosomy 7), #12 (t(15;17)) and #13 (t(8;21)). Patients with a complete clinical data set were included in the survival analyses (Figure 2). The mean actuarial OS and DFS probabilities at 60 months of the patients with favourable cytogenetics were 62% (±8.7%) and 50% (±2.4%), respectively. AML patients included in cluster #5 had intermediate survival (OS 27% and EFS 32%), whereas patients from cluster #10 showed poor treatment response (OS 6% (P=0.001) and EFS 18% (P=0.004)) mainly as a result of increased relapse incidence (Figure 2C).

Discussion

The results of the study presented here show profound diagnostic

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impact of expression profiling. Among AML with considerable genetic diversity, expression profiling provides an approach to distinguish these highly variable genetic subsets into clusters with distinct signatures. Patients with AML were classified in 16 groups based on their gene expression profiles by unsupervised Pearson's correlation coefficient analyses. The results show that each of the assigned clusters represents true AML subgroups with specific molecular signatures.

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Firstly, all cases with t(8;21) (AML1/ETO), inv(16) (CBFβ/MYH11) or t(15;17) (PML/RARα), including patients that could not be recognized by karyotyping, could be clustered in three separate clusters with unique gene expression profiles. Unique correlations between gene expression profiles and favourable cytogenetic aberrations have been shown in the prior art (Debernardi et al., 2003; Schoch et al., 2002), however, here we demonstrate that these patients can even be recognized with high accuracy within a representative cohort of AML patients.

Secondly, Significance Analyses of Microarrays (SAM) and Prediction Analyses of Microarrays (PAM), showed a strong concordance between the specific genes identified for the different assigned clusters, demonstrating that we identified truly discriminative genes for all the clusters that we assigned. For instance, we identified two distinct clusters (#4 and #15) with overlapping signatures, which both included cases with normal karyotypes and mutations in $cEBP\alpha$. Multiple genes appeared to be downregulated in both subclasses but were unaffected in any other AML subgroup.

Thirdly, the discriminative genes identified by SAM and PAM may in addition reveal specific functional pathways critical for the pathophysiology of AML. This is suggested by the identification of several functionally important genes implicated in specific subtypes of AML, such as the IL5R α in AML with t(8;21) (Touw *et al.*, 1991) and the bona fide FLT3/STAT5 targets $IL2R\alpha$ (Kim *et al.*, 2001) and PIM1 (Lilly *et al.*, 1992) in AML with FLT3 ITD

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mutations.

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Five clusters (#5, #9, #10, #12 and #13) 20 or more cases were evaluated in relation to outcome of therapy. As expected, clusters #9 (CBFβ/MYH11), #12 (PML/RARα) and #13 (AML1/ETO), comprised cases with a favorable response to therapy. However, cases that belong to cluster #10 showed a distinct poor outcome. Patients in this cluster could be predicted with high accuracy in an independent validation set with a minimal set of genes. The high frequency of poor prognostic markers, e.g., -7(q), -5(q), t(9;22) or high EVI1 is in agreement with the observation that this cluster represents a badrisk AML group. However, since the cluster contains AML cases with a variety of genetically defined poor risk markers and since a significant portion of the cases did not express any of these lesions, this suggests that a unique pathway represented by the molecular signature of this cluster of AML patients is associated with bad outcome.

This hypothesis is further strengthened by the fact that large numbers of cases with the same poor-risk markers were present in other clusters (#1, #2, #8 and #16). Analysis of the genes up- or downregulated in AML cases from cluster #10 may predict the pathway(s) involved the pathophysiology of this subgroup of AML patients. This might also shed light on the findings that the other cases with distinct poor-prognostic markers are grouped in different clusters. Unfortunately, these latter groups were too small for an accurate analysis of treatment outcome.

The 44 AML patients in cluster #5 showed an intermediate survival estimate. Since these cases belong to AML FAB-M4 or -M5 subtype, it is possible that monocyte/macrophage related genes mainly drove clustering of these cases. Unsupervised clustering of larger numbers of only AML FAB-M4 or -M5 cases with a normal karyotype may result in the identification of specific subgroups with unique gene expression profiles and perhaps variable prognosis.

Three clusters mainly consisting of patients with normal karyotype

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were identified. The majority of patients in two of those clusters (#2 and #6) were also characterized by *FLT3* ITD mutations, whereas patients in cluster #11, with a discriminative molecular signature, did not contain any consistent abnormality.

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Two clusters (#1 and #16) were recognized, which harbored 11q23 abnormalities, representing defects involving the mixed-lineage leukemia gene. The reason for the separation of these two subgroups is most likely caused by different additional genetic defects in the cases of the distinct clusters, causing different gene expression profiles. In cluster #1 this abnormality may be the frequently observed high expression of EVI1, which is not apparent in AML cases from cluster #16. A similar explanation may hold for AML cases in clusters #4 and #15, both comprising $cEBP\alpha$ mutant cases, AML patients in clusters #1 and #10 (high EVI1 expression), or patients in clusters #8 and #10 with frequent monosomy 7. Given the fact that each of these clusters expressed such a distinct molecular signature most probably means that in the cases without the characteristic genetic lesion, other currently unidentified mutations affecting the same pathways are responsible for the genetic profiles.

Internal tandem duplications (ITD) in the *FLT3* gene adversely affect clinical outcome (Levis & Small, 2003). The molecular signature induced by the constitutively activated the FLT3 receptor appears not strong enough to distinguish *FLT3* ITD carrying AML patients from the other cases. However, the clustering of *FLT3* ITD positive patients within assigned clusters, as is the case in the APL subgroup (cluster #12), demonstrates that the presence of *FLT3* ITD results in different biological entities within one type of disease.

To this end, our study demonstrates that cytogenetically known as well as new clusters of AML with characteristic gene expression signatures can be identified with one single assay. The quality of genome-wide analysis will further advance with the availability of novel whole genome arrays, improved sequence annotation and the development of more sophisticated

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protocols and software, allowing analysis of subtle differences in gene expression and comprehensive pathway prediction. These studies, while augmenting our understanding of the pathways involved in pathophysiology of AML, will result in improved diagnostics and possibly lead the way to the development anti-cancer drugs that interfere with disease related pathways.

EXAMPLE 2

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Analyses of novel AML patients

10 Patients and cell samples

Eligible patients have a diagnosis of primary AML, confirmed by cytological examination of blood and bone marrow. Blasts and mononuclear cells should be purified by Ficoll-Hypaque (Nygaard, Oslo, Norway) centrifugation. Add 1:1 diluted peripheral blood or bone marrow 1:4 diluted both in PBS up to 20-25 ml on to 15 ml Ficoll-Hypaque. Spin 15 minutes at 1880rpm. Collect interphase with mononuclear cells and wash twice with PBS (total volume 50ml, 8 minutes 2000 rpm). The pellet contains the mononuclear cells, including the blast cells. As a result, the AML samples should contain 80-100 percent blast cells, regardless of the blast count at diagnosis. 30.106 cells/ml should be frozen in 1vol PBS/1 vol heat inactivated FCS/0.5 vol DMSO stored in liquid nitrogen.

RNA isolation and quality control

After thawing, cells were washed once with Hanks balanced salt solution. High quality total RNA should extracted by lysis with guanidinium isothiocyanate followed by cesium chloride gradient purification. RNA concentration, quality and purity should be examined using the RNA 6000 Nano assay on the Agilent 2100 Bioanalyzer (Agilent, Amstelveen, The Netherlands). None of the samples should show RNA degradation (28S/18S rRNA ratio ≥ 2) or contamination by DNA.

Gene profiling and quality control

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Ten ug of total RNA should be used to prepare antisense biotinylated RNA. Single-stranded cDNA and double-stranded cDNA should be synthesized according to the manufacturer's protocol (Invitrogen Life Technologies, Breda, The Netherlands) using the T7-(dT)24-primer (Genset Corp, Paris, France). In vitro transcription should be performed with biotin-11-CTP and biotin-16-UTP (Perkin Elmer, Hoofddorp, The Netherlands) and the MEGAScript T7 labeling kit (Ambion, Cambridgeshire, UK). Double-stranded cDNA and cRNA should be purified and fragmented with the GeneChip® Sample Cleanup Module (Affymetrix, Santa Clara, CA). Biotinylated RNA should be hybridized to the Affymetrix U133A GeneChip® (45°C for 16 hours). Samples should be analyzed using Affymetrix U133A or U133 Plus2.0 GeneChips®. The U133A GeneChip® contains 22283 probe sets, representing approximately 13000 genes. These probe sets can also be selected from the U133 Plus2.0 GeneChip®. Staining, washing and scanning procedures should be carried out as described in the GeneChip® Expression Analysis Technical Manual (Affymetrix, Santa Clara, CA). All GeneChips® should be visually inspected for irregularities. The global method of scaling/normalization should be applied and the differences between the scaling/normalization factors of all GeneChips® up to the Target Gene Intensity of 100 (reference value n=285: scaling factor = 0.70, SD 0.26). All additional measures of quality - percent genes present (reference value n=285: 50.6 ±3.8), actin 3' to 5' ratio (reference value n=285: 1.24 ±0.19) and GAPDH 3'to 5' ratio (reference value n=285: 1.05 ±0.14) - should indicate high overall sample and assay quality.

Reference data set

A reference data set (gene expression data and detailed clinical and molecular data) of 285 AML patients should be downloaded from the Gene Expression Omnibus (www.ncbi.nlm.nih.gov/geo, accession number GSE1159).

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Data normalization, analysis and visualization

All intensity values (reference set (n=285) and new AML patients to be included) should be scaled to an a verage value of 100 per GeneChip® according to the method of global scaling/normalization, available in the Affymetrix Microarray Suite (MA.S5.0). All other setting should be default according to the manufacturer.

As our methods reliably identify samples with an average intensity value >30 but do not reliably discriminate v alues from 0 - <30, these values should be set to 30.

For each probe set the geometric mean of the hybridization intensities of all patient samples should calculated. The level of expression of each probe set in every sample was determined relative to this geometric mean and transformed to \log_2 to ascribe equal weight to gene-expression levels with similar relative distances to the geometric mean. The transformed expression data should be subsequently imported into Omniviz.

Pearson's Correlation Visua Zization tool of Omniviz (Maynard, MA (version 3.6)) – The Omniviz package should be used to perform and visualize unsupervised cluster analysis. The clustering of molecularly recognizable specific groups of patients should be investigated with the 2856 probe sets (Table 1) taking the reference set (n=285) and new patients to be analysed into account.

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5 Table 1. About 2856 genes used for classifying AML of 286 patients into defined clusters as identified in Correlation View

10	Affymetrix probe set id	gene symbol	unigene ID
	117 at	HSPA6	Hs.3268
	1405_i_at	CCL5	Hs.241392
	1598_g_at	GAS6	Hs.437710
	200067 x at	SNX3	Hs.12102
15	200075 s at	GUK1	Hs.376933
	200099_s_at		//
	200602_at	APP	Hs.177486
	200606_at	DSP	Hs.349499
	200612_s_at	AP2B1	Hs.370123
20	200616_s_at	KIAA0152	Hs.181418
	200628_s_at	WARS	Hs.82030
	200629_at	WARS	Hs.82030
	200632_s_at	NDRG1	Hs.318567
	200644_at	MLP	Hs.75061
25	200648_s_at	GLUL	Hs.442669
	200660_at	S100A11	Hs.417004
	200661_at	PPGB	Hs.118126
	200665_s_at	SPARC	Hs.111779
	200671_s_at	SPTBN1	Hs.205401
30	200672_x_at	SPTBN1	Hs.205401
	200675_at	CD81	Hs.54457
	200678_x_at	GRN	Hs.180577
	200696_s_at	GSN	Hs.446537
~~	200697_at	HK1	Hs.118625
35	200703_at	DNCL1	Hs.5120
	200704_at	LITAF	Hs.76507
	200706_s_at	LITAF	Hs.76507
	200736_s_at	GPX1	Hs.76686
40	200762_at	DPYSL2	Hs.173381
40	200765_x_at	CTNNA1	Hs.254321
	200766_at	CTSD	Hs.343475
	200771_at	LAMC1	Hs.432855

	200720 ** a*	GNAS	Hs.157307
	200780_x_at	ANXA5	Hs.145741
5	200782_at		
i)	200784_s_at	LRP1	Hs.162757
	200785_s_at	LRP1	Hs.162757
	200791_s_at	IQGAP1	Hs.1742
	200795_at	SPARCL1	Hs.75445
	200796_s_at	MCL1	Hs.86386
10	200799_at	HSPA1A	$\mathrm{Hs.75452}$
	200800_s_at	HSPA1A	Hs.75452
	200808_s_at	ZYX	Hs.75873
	200832_s_at	SCD	Hs.119597
	200838_at	CTSB	Hs.135226
15	200839_s_at	CTSB	Hs.135226
	200853_at	H2AFZ	Hs.119192
	200871_s_at	PSAP	Hs.406455
		S100A10	Hs.143873
	200872_at	EPAS1	Hs.8136
20	200878_at		
20	200895_s_at	FKBP4	Hs.848
	200897_s_at	KIAA0992	Hs.194431
	200907_s_at	KIAA0992	Hs.194431
	200921_s_at	BTG1	Hs.255935
~ =	200923_at	LGALS3BP	$\mathrm{Hs.79339}$
25	200931_s_at	VCL	$\mathrm{Hs.75350}$
	200952_s_at	CCND2	Hs.376071
	200953_s_at	CCND2	Hs.376071
	200962_at	RPL31	Hs.375921
	200965_s_at	ABLIM1	Hs.442540
30	200981_x_at	GNAS	Hs.157307
00	200982_s_at	ANXA6	Hs.412117
	200983_x_at	CD59	Hs.278573
	200985 s at	CD59	Hs.278573
	200985_s_at 200986_at	SERPING1	Hs.384598
35		HIF1A	Hs.412416
00	200989_at		
	200991_s_at	SNX17	Hs.278569
	200998_s_at	CKAP4	Hs.74368
	200999_s_at	CKAP4	Hs.74368
40	201005_at	CD9	Hs.387579
40	201008_s_at	TXNIP	Hs.179526
	201012_at	ANXA1	Hs.287558
	201013_s_at	PAICS	Hs.444439
	201015_s_at	JUP	Hs.2340
	201024_x_at	IF2	Hs.158688
45	201034_at	ADD3	Hs.324470
	201037_at	PFKP	Hs.26010
	201041_s_at	DUSP1	Hs.171695
	201043_s_at	ANP32A	Hs.124977
	201044_x_at	DUSP1	Hs.171695
50	201047_x_at	RAB6A	Hs.5636
00	201050_at	PLD3	Hs.74573
	201050_at 201052_s_at	PSMF1	Hs.437495
	201058_s_at	MYL9	Hs.433814
==	201060_x_at	STOM	Hs.439776
55	201061_s_at	STOM	Hs.439776
	201069_at	MMP2	Hs.367877
	201105_at	LGALS1	Hs.407909
	201107_s_at	THBS1	Hs.164226
	201108_s_at	THBS1	Hs.164226
60	201109_s_at	THBS1	Hs.164226
	201110_s_at	THBS1	Hs.164226
	201123_s_at	EIF5A	Hs.310621
	201125_s_at	ITGB5	Hs.149846
	201131_s_at	CDH1	Hs.194657
65	201136_at	PLP2	Hs.77422
	201137_s_at	HLA-DPB1	Hs.368409
	201141_at	GPNMB	Hs.389964
	201111_00		110,00000T

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		,	
	201160_s_at	CSDA	Hs.221889
	201161_s_at	CSDA	Hs.221889
5	201162_at	IGFBP7	Hs.435795
0	201163_s_at	IGFBP7	Hs.435795
	201169 s_at	BHLHB2	Hs.171825
	201105_s_at 201170_s_at	BHLHB2	Hs.171825
	201170_s_at 201174_s_at	TERF2IP	Hs.274428
10	201174_3_at	FBXO7	Hs.5912
10	201176_at 201189_s_at	ITPR3	Hs.77515
	201193_s_at	IDH1	Hs.11223
		SLC7A5	Hs.184601
	201195_s_at	CSTB	Hs.695
15	201201_at	CTBP2	Hs.171391
19	201218_at	CTBP2	Hs.171391
	201220_x_at	RAD23B	Hs.159087
	201222_s_at	RAD23B RAD23B	Hs.159087
	201223_s_at		Hs.6196
20	201234_at	ILK	Hs.78629
20	201242_s_at	ATP1B1	Hs.169902
	201249_at	SLC2A1	Hs.169902
	201250_s_at	SLC2A1	
	201251_at	PKM2	Hs.198281
0.5	201272_at	AKR1B1	Hs.75313
25	201285_at	MKRN1	Hs.7838
	201291_s_at	TOP2A	Hs.156346
	201294_s_at	WSB1	Hs.315379
	201295_s_at	WSB1	Hs.315379
00	201300_s_at	PRNP	Hs.438582
30	201301_s_at	ANXA4	Hs.422986
	201302_at	ANXA4	Hs.422986
	201307_at	FLJ10849	Hs.386784
	201309_x_at	C5orf13	Hs.508742
0 =	201313_at	ENO2	Hs.146580
35	201324_at	EMP1	Hs.306692
	201325_s_at	EMP1	Hs.306692
	201328_at	ETS2	Hs.292477
	201329_s_at	ETS2	Hs.292477
40	201333_s_at	ARHGEF12	Hs.413112
4 0	201334_s_at	ARHGEF12	Hs.413112
	201348_at	GPX3	Hs.386793
	201360_at	CST3	Hs.304682
	201373_at	PLEC1	Hs.79706
4 -	201389_at	ITGA5	Hs.149609
45	201392_s_at	IGF2R	Hs.76473
	201393_s_at	IGF2R	Hs.76473
	201412_at	LRP10	Hs.28368
	201416_at	SOX4	Hs.357901
~ 0	201417_at	SOX4	Hs.357901
50	201418_s_at	SOX4	Hs.357901
	201422_at	IFI30	Hs.14623
	201425_at	ALDH2	Hs.436437
	201426_s_at	VIM	Hs.435800
,- - -	201427_s_at	SEPP1	Hs.275775
55	201431_s_at	DPYSL3	Hs.150358
	201445_at	CNN3	Hs.194662
	201459_at	RUVBL2	Hs.6455
	201462_at	KIAA0193	Hs.75137
00	201464_x_at	JUN	Hs.78465
60	201465_s_at	JUN	Hs.78465
	201466_s_at	JUN	Hs.78465
	201473_at	JUNB	Hs.400124
	201487_at	CTSC	Hs.128065
a-	201497_x_at	MYH11	Hs.78344
65	201506_at	\mathbf{TGFBI}	Hs.421496
	201508_at	IGFBP4	Hs.1516
	201518_at	CBX1	Hs.77254

			ē
	201522_x_at	SNRPN	Hs.48375
	201521_at	ZFP36	Hs.343586
5	-		
U	201536_at	na	Hs.181046
	201539_s_at	FHL1	Hs.421383
	201540_at	FHL1	Hs.421383
	201548_s_at	PLU-1	Hs.143323
10	201549_x_at	PLU-1	Hs.143323
10	201550_x_at	ACTG1	Hs.14376
	201563_at	SORD	$\mathrm{Hs.878}$
	201564_s_at	FSCN1	Hs.118400
	201565_s_at	ID2	Hs.180919
	201566_x_at	ID2	Hs.180919
15	201579_at	FAT	Hs.166994
	201590_x_at	ANXA2	Hs.437110
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	201599_at	OAT	Hs.75485
	201601_x_at	IFITM1	Hs.458414
20	201631_s_at	IER3	Hs.76095
	201644_at	TSTA3	Hs.404119
	201655_s_at	HSPG2	Hs.211573
	201656_at	ITGA6	Hs.212296
		TIMP1	Hs.446641
25	201666_at	GJA1	
20	201667_at	MARCKS	Hs.74471
	201668_x_at		Hs.318603
	201669_s_at	MARCKS	Hs.318603
	201670_s_at	MARCKS	Hs.318603
00	201688_s_at	TPD52	Hs.162089
30	201689_s_at	$ ext{TPD52}$	Hs.162089
	201690_s_at	TPD52	Hs.162089
	201693_s_at	EGR1	Hs.326035
	201694_s_at	EGR1	Hs.326035
	201695_s_at	NP	Hs.75514
35	201700_at	CCND3	Hs.83173
	201711_x_at	RANBP2	Hs.199179
	201714_at	TUBG1	Hs.21635
	201720_s_at	LAPTM5	Hs.436200
	201734_at	CLCN3	Hs.372528
40	201735_s_at	CLCN3	Hs.372528
	201739_at	SGK	Hs.296323
	201743_at	CD14	Hs.75627
	201746_at	TP53	Hs.426890
	201752_s_at	ADD3	Hs.324470
45	201752_s_at 201753_s_at	ADD3	Hs.324470
40		DHCR7	Hs,11806
	201790_s_at		
	201791_s_at	DHCR7	Hs.11806
	201792_at	AEBP1	Hs.439463
K٥	201795_at	LBR	Hs.435166
50	201798_s_at	FER1L3	Hs.362731
	201809_s_at	ENG	Hs.76753
	201810_s_at	SH3BP5	Hs.109150
	201811_x_at	SH3BP5	Hs.109150
~ ~	201824_at	RNF14	Hs.170926
55	201831_s_at	VDP	Hs.325948
	201839_s_at	TACSTD1	Hs.692
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	201842_s_at	EFEMP1	Hs.76224
	201850_at	CAPG	Hs.82422
60	201852_x_at	COL3A1	Hs.443625
	201858_s_at	PRG1	Hs.1908
	201859_at	PRG1	Hs.1908
	201860 s at	PLAT	Hs.274404
	201883_s_at	B4GALT1	Hs.396798
65	201887 at	IL13RA1	Hs.285115
	201888_s_at	IL13RA1	Hs.285115
	201890_at	RRM2	Hs.226390
			110.22.000

	201893_x_at	DCN	Hs.156316
	201909_at	RPS4Y	Hs.180911
5	201912_s_at	GSPT1	Hs.2707
•	201923_at	PRDX4	Hs.83383
	201938_at	CDK2AP1	Hs.433201
	201944_at	HEXB	Hs.69293
	201952_at	ALCAM	Hs.10247
10	201963_at	FACL2	Hs.406678
10	201968_s_at	PGM1	Hs.1869
	201995_at	EXT1	Hs.184161
	202007_at	NID	Hs.356624
		PPP1R15A	Hs.76556
15	202014_at		
10	202016_at	MEST	Hs.416498
	202017_at	EPHX1	Hs.89649
	202018_s_at	LTF	Hs.437457
	202059_s_at	KPNA1	Hs.161008
90	202068_s_at	LDLR	Hs.213289
20	202071_at	SDC4	Hs.252189
	202073_at	OPTN	Hs.390162
	202074_s_at	OPTN	Hs.390162
	202083_s_at	SEC14L1	Hs.75232
0 =	202085_at	TJP2	Hs.75608
25	202086_at	MX1	Hs.436836
	202087_s_at	CTSL	Hs.418123
	202088_at	LIV-1	Hs.79136
	202096_s_at	BZRP	Hs.202
	202107_s_at	MCM2	Hs.57101
30	202112_at	VWF	Hs.440848
	202119_s_at	CPNE3	Hs.14158
	202124_s_at	ALS2CR3	Hs.154248
	202125_s_at	ALS2CR3	Hs.154248
	202129_s_at	RIOK3	Hs.209061
35	202130_at	RIOK3	Hs.209061
	202131_s_at	RIOK3	Hs.209061
	202145_at	LY6E	Hs.77667
	202153_s_at	NUP62	Hs.437023
	202177_at	GAS6	Hs.437710
40	202191_s_at	GAS7	Hs.226133
	202192_s_at	GAS7	Hs.226133
	202193_at	LIMK2	Hs.278027
	202201_at	BLVRB	Hs.76289
	202203_s_at	AMFR	Hs.295137
45	202204_s_at	\mathbf{AMFR}	Hs.295137
	202206_at	ARL7	Hs.111554
	202207_at	ARL7	Hs.111554
	202208_s_at	ARL7	Hs.111554
	202219_at	SLC6A8	Hs.388375
50	202234_s_at	SLC16A1	Hs.75231
	202236_s_at	SLC16A1	Hs.75231
	202237_at	NNMT	Hs.364345
	202238_s_at	\mathbf{NNMT}	Hs.364345
	202241_at	C8FW	Hs.444947
55	202242_at	TM4SF2	Hs.439586
	202252_at	RAB13	Hs.151536
	202265_at	BMI1	Hs.380403
	202269_x_at	GBP1	Hs.62661
	202270_at	GBP1	Hs.62661
60	202283_at	SERPINF1	Hs.173594
	202284_s_at	CDKN1A	Hs.370771
	202286_s_at	TACSTD2	Hs.23582
	202291_s_at	MGP	Hs.365706
	202295_s_at	CTSH	Hs.114931
65	202310_s_at	COL1A1	Hs.172928
	202336_s_at	PAM	Hs.352733
	202340_x_at	NR4A1	Hs.1119

	202345_s_at	FABP5	Hs.408061
	202364_at	MXI1	Hs.118630
5	202379_s_at	NKTR	Hs.369815
Ū	202388_at	RGS2	Hs.78944
	202391_at	BASP1	Hs.79516
	202395_at	NSF	Hs.431279
	202403_s_at	COL1A2	Hs.232115
10	202409_at	na	Hs.251664
	202411_at	IFI27	Hs.278613
	202425_x_at	PPP3CA	Hs.272458
	202426_s_at	RXRA	Hs.20084
	202429_s_at	PPP3CA	Hs.272458
15	202431_s_at	MYC	$\mathrm{Hs.}202453$
	202435_s_at	CYP1B1	Hs.154654
	202436_s_at	CYP1B1	Hs.154654
	202437_s_at	CYP1B1	Hs.154654
	202443_x_at	NOTCH2	Hs.8121
20	202452_at	ZYG	Hs.29285
	202456_s_at	ZYG	Hs.29285
	202457_s_at	PPP3CA	Hs.272458
	202459_s_at	LPIN2	Hs.437425
	202460_s_at	LPIN2	Hs.437425
25	202464_s_at	PFKFB3	Hs.195471
	202478_at	TRB2	Hs.155418
	202479_s_at	TRB2	Hs.155418
	202481_at	SDR1	Hs.17144
	202492_at	FLJ22169	Hs.323363
30	202497_x_at	SLC2A3	Hs.419240
	202498_s_at	SLC2A3	Hs.419240
	202499_s_at	SLC2A3	Hs.419240
	202500_at	DNAJB2	Hs.77768
~ ~	202503_s_at	KIAA0101	Hs.81892
35	202510_s_at	TNFAIP2	Hs.101382
	202523_s_at	SPOCK2	Hs.436193
	202524_s_at	SPOCK2	Hs.436193
	202545_at	PRKCD	Hs.155342
40	202546_at	VAMP8	Hs.172684
4 0	202548_s_at	ARHGEF7	Hs.172813 Hs.170752
	202551_s_at	CRIM1	Hs.2006
	202554_s_at	GSTM3	Hs.386078
	202555_s_at	MYLK	Hs.163111
45	202565_s_at	SVIL SVIL	Hs.163111
40	202566_s_at	HSPA1A	Hs.274402
	202581_at	AK1	Hs.76240
	202587_s_at	TYMS	Hs.87491
	202589_at	NRIP1	Hs.155017
50	202599_s_at	NRIP1	Hs.155017
50	202600_s_at	EPS8	Hs.2132
	202609_at 202614_at	C4orf1	Hs.364615
		CABIN1	Hs.435798
	202624_s_at 202626_s_at	LYN	Hs.80887
55	202627_s_at	SERPINE1	Hs.414795
00	202628_s_at	SERPINE1	Hs.414795
	202625_s_at 202637_s_at	ICAM1	Hs.168383
	202638_s_at	ICAM1	Hs.168383
	202643_s_at	TNFAIP3	Hs.211600
60	202644_s_at	TNFAIP3	Hs.211600
50	202660_at		Hs.406751
	202600_at 202671_s_at	MGC15873	Hs.284491
	202671_s_at	ATF3	Hs.460
	202686_s_at	AXL	Hs.83341
65	202687_s_at	TNFSF10	Hs.387871
	202688_at	TNFSF10	Hs.387871
	202704_at	TOB1	Hs.178137

	202708_s_at	HIST2H2BE	Hs.2178
	202718 at	IGFBP2	Hs.433326
5	202720 at	TES	Hs.129129
•	202724_s_at	FOXO1A	Hs.170133
	202728_s_at	LTBP1	Hs.241257
	202729_s_at	LTBP1	Hs.241257
	202741_at	PRKACB	Hs.156324
10	202742 s. at	PRKACB	Hs.156324
	202746_at	ITM2A	Hs.17109
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	202748 at	GBP2	Hs.386567
	202759 s at	AKAP2	Hs.42322
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	202761_s_at	SYNE2	Hs.444069
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	202878_s_at	C1QR1	Hs.97199
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	202888_s_at	ANPEP	Hs.1239
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	203065_s_at	CAV1	Hs.74034
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	204099_at	SMARCD3	Hs.44445
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	204257_at	FADS3	Hs.21765
	204259_at	MMP7	Hs.2256
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	204447_at	ProSAPiP1	Hs.90232
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	204457_s_at	GAS1	$\mathrm{Hs.65029}$
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55	204494_s_at	LOC56905	Hs.306331
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	204790_at	MADH7	Hs.370849
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55	205193_at	MAFF	Hs.51305
•	205200_at	TNA	Hs.65424
	205205_at	RELB	Hs.307905
	205207, at	IL6	Hs.130210
	205213_at	CENTB1	Hs.337242
60	205214_at	STK17B	Hs.88297
	205220_at	HM74	Hs.458425
	205227_at	IL1RAP	Hs.143527
	205229_s_at	COCH	Hs.21016
	205230_at	RPH3A	Hs.21239
65	205237_at	FCN1	Hs.440898
	205239_at	AREG	Hs.270833
	205240_at	LGN	Hs.278338

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	205249_at	EGR2	Hs.1395
5	205254 x at	TCF7	Hs.169294
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	205262_at	KCNH2	Hs.188021
	205266_at	LIF	Hs.2250
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	205278_at	GAD1	Hs.420036
	205281_s_at	PIGA	Hs.51
	205289_at	BMP2	Hs.73853
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	205328_at	CLDN10	Hs.26126
	205330_at	MN1	Hs.268515
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	205349_at	GNA15	Hs.73797
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	205361_s_at	PFDN4	Hs.91161
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20	205389_s_at	ANK1	Hs.443711
	205390_s_at	ANK1	Hs.443711
	205391 x at	ANK1	Hs.443711
	205392_s_at	CCL15	Hs.272493
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	205570_at	PIP5K2A	Hs.108966
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65	205599_at	TRAF1	Hs.438253
	205608_s_at	ANGPT1	Hs.2463
	205609_at	ANGPT1	Hs.2463

		1001	TT 000105
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_	205614_x_at	MST1	Hs.349110
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	205743_at	STAC	Hs.56045
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	205769_at	SLC27A2	Hs.11729
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50	205801_s_at	RASGRP3	
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	205859_at	LY86	Hs.184018
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	205882_x_at	ADD3	Hs.324470
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	206067_s_at	WT1	Hs.1145
	206070_s_at	EPHA3	Hs.123642
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55	206310_at	SPINK2	Hs.98243
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40	206622_at	TRH	Hs.182231
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	-	SMCY	
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	206726_at	PGDS	Hs.128433
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	206877_at	MAD	Hs.379930
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	206918_s_at	RBM12	Hs.166887
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	206932_at	CH25H	Hs.47357
	206934_at	SIRPB1	Hs.194784
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	206940_s_at	POU4F1	Hs.458303
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	206978_at	CCR2	Hs.395
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	207001_x_at	DSIPI	Hs.420569
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	207072 at	IL18RAP	Hs.158315
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	207224_s_at	SIGLEC7	Hs.274470
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	207269_at	DEFA4	Hs.2582
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	207357_s_at	GALNT10	Hs.13785
	207358_x_at	MACF1	Hs.372463
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	207384_at	PGLYRP	Hs.137583
65	207387_s_at	GK	Hs.1466
	207389_at	GP1BA	Hs.1472
	207419_s_at	RAC2	Hs.301175
			

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5	207435 s.at	SRRM2	Hs.433343
Ü	207459_x_at	GYPB	Hs.438658
	207467_x_at	CAST	Hs.440961
	207496 at	MS4A2	Hs.386748
	207509_s_at	LAIR2	Hs.43803
10	207511_s_at	CGI-57	Hs.4973
	207522_s_at	ATP2A3	Hs.5541
	207526_s_at	IL1RL1	Hs.66
	207533_at	CCL1	Hs.72918
	207535 s_at	NFKB2	Hs.73090
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	207542_s_at	AQP1	Hs.76152
	207550_at	MPL	Hs.84171
	207571_x_at	Clorf38	Hs.10649
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	207802_at	SGP28	Hs.404466
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	207827_x_at	SNCA	Hs.76930
40	207836_s_at	RBPMS	Hs.195825
	207838_x_at	PBXIP1	Hs.8068
	207850_at	CXCL3	Hs.89690
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	207911_s_at	TGM5	Hs.129719
	207938_at	PI15	Hs.129732
	207978_s_at	NR4A3	Hs.279522
50	207979_s_at	CD8B1	Hs.405667
	207983_s_at	${f STAG2}$	Hs.8217
	208018_s_at	HCK	Hs.89555
	208029_s_at	LAPTM4B	Hs.296398
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	208067_x_at	UTY	Hs.115277
	208071_s_at	LAIR1	Hs.407964
	208078_s_at	TCF8	Hs.232068
	208091_s_at	DKFZP564K0822	Hs.4750
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	208370_s_at	DSCR1	Hs.282326
1 -	208416_s_at	SPTB	Hs.438514
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	208438_s_at	FGR	Hs.1422
	208443_x_at	SHOX2	Hs.55967
	208450_at	LGALS2	Hs.113987
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	208470_s_at	$_{ m HP}$	Hs.403931
	208476_s_at	FLJ10210	Hs.171532
	208488_s_at	CR1	Hs.334019
~ ~	208490_x_at	HIST1H2BF	Hs.182137
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	208553_at	HIST1H1E	Hs.248133
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35	208581_x_at	MT1X	Hs.374950
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50	213182_x_at	CDKN1C	Hs.106070
50	213193_x_at	TRB@	Hs.419777
	213194_at	ROBO1	Hs.301198
	213201_s_at	TNNT1	Hs.73980
	213212_x_at	+ CTC -	Hs.459128 // est
==	213214_x_at	ACTG1	Hs.14376
55	213217_at	ADCY2	Hs.414591
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	213241_at	PLXNC1	Hs.286229
	213258_at	TFPI	Hs.102301
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	213275_x_at	CTSB	Hs.135226
	213288_at	LOC129642	$\mathrm{Hs.90797}$
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5	213375_s_at	CG018	Hs.277888
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	21 3395_at	MLC1	Hs.74518
	21 3413_at	SBLF	Hs.54961
	213415_at	CLIC2	Hs.54570
10	213410_at 213418_at	HSPA6	Hs.3268
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	21 3425_s_at 21 3435_at	SATB2	Hs.412327 //
	21 3435_at 21 3437_at	RIPX	Hs.7972
	21 3439_x_at		Hs.500197 // est
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	21 3479_at	DOCK3	Hs.7022
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20	21 3484_at	na FLJ00133	Hs.7949
	21.3488_at		Hs.408182
	21 3492_at	COL2A1	Hs.435211 //
	21 3502_x_at	LOC91316 ANXA2	Hs.437110
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	21 3515_x_at	HBG2	Hs.302145
	21 3521_at	PTPN18	Hs.210913
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	21 3541_s_at	ERG	Hs.45514
	21 3545_x_at	SNX3 SLC18A2	Hs.12102
	21 3549_at		Hs.50458
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	21 3572_s_at	SERPINB1	Hs.381167
	21 3605_s_at	na WETD 1	Hs.166361 //
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	21 3629_x_at	MT1F	Hs.438737
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	21 3757_at	EIF5A PENK	
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	21 3823_at	HOXA11	Hs.249171
	21 3825_at	OLIG2	Hs.176977
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	21 3841_at	na Waganaa	Hs.301281 //
	21 3842_x_at	WBSCR20C	Hs.436034
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	213888_s_at 213891 s at	TCF4	Hs.359289
	21 3894 at	LOC221981	Hs.23799 //
65	21 3906_at	MYBL1	Hs.300592 //
50	213906_at 213908_at	LOC339005	Hs.212670 //
	213905_at 213915_at	NKG7	Hs.10306
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0	213960_at	na	Hs.185701 //
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	213988 s at	SAT	Hs.28491
	213994_s_at	SPON1	Hs.5378
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	214032_at	ZAP70	Hs.234569
	214039 s_at	LAPTM4B	Hs.296398
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	214061_at	MGC21654	Hs.95631
	214063_s_at	TF	Hs.433923
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	214121_x_at	ENIGMA	Hs.436339
	214131_at	CYorf15B	$\mathrm{Hs.}145010$
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	214153_at	ELOVL5	$\mathrm{Hs.343667}$
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	214203_s_at	PRODH	Hs.343874
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	214230_at	CDC42	Hs.355832
	214235_at	CYP3A5	Hs.150276
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40	214273_x_at	C16orf35	Hs.19699
	214290_s_at	HIST2H2AA	Hs.417332
	214295_at	KIAA0485	Hs.89121 //
	214297_at	CSPG4	Hs.436301
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	214470_at	KLRB1	Hs.169824
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	214627_at	EPX	Hs.46295
ΩΛ	214637_at	OSM	Hs.248156
20	214651_s_at	HOXA9	Hs.127428
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	214667_s_at	TP53I11	Hs.433813 //
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	214770_at	MSR1	Hs.436887
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	214805_at	EIF4A1	Hs.129673
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	214870_x_at		//
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	214920_at	LOC221981	Hs.23799 //
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	215034_s_at	BCL2L1	Hs.305890
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	215049_x_at	AIF1	Hs.76364
	215051_x_at		Hs.127826
	215054_at	EPOR	Hs.28777 //
CO	215071_s_at	COT DAT	
60	215076_s_at	COL3A1	Hs.443625
	215078_at	SOD2	Hs.384944
	215089_s_at	RBM10	Hs.348276
	215111_s_at	TSC22	Hs.114360
C F	215116_s_at	DNM1	Hs.436132
65	215118_s_at	MGC27165	Hs.366
	215121_x_at		Hs.356861
	215123_at		Hs.375005 //

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	215137_at		Hs.467531 // est
	215143_at	FLJ36166	Hs.351178 //
5	215146_s_at	KIAA1043	Hs.387856
•	215150_at	DKFZp451J1719	Hs.391944 //
	215163_at		Hs.203349 //
	215176_x_at		Hs.503443 //
	- -	ITGA6	Hs.212296
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	215200_x_at	na	Hs.456817 //
	215204_at		Hs.288575 //
	215214_at		Hs.449579 //
	215222_x_at	MACF1	Hs.372463
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	215248_at	GRB10	Hs.81875
	215284_at		Hs.12432 //
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	215306_at		Hs.161283 //
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	215320_at	DKFZP434M131	Hs.189296 //
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	215379_x_at		
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	215411_s_at	C6orf4	Hs.437508
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	215438_x_at	GSPT1	$\mathrm{Hs.2707}$
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	215485_s_at	ICAM1	Hs.168383
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	215571_at		Hs.287415 //
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	215599_at		
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	215663_at	MBNL1	Hs.28578
55	215666_at	HLA-DRB4	$\mathrm{Hs.449633}$
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	215692_s_at	C11orf8	Hs.432000
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	215733_x_at	CTAG2	Hs.87225
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	215806_x_at	TRGC2	Hs.385086

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	215836_s_at	PCDHGC3	Hs.283794
	215838_at	LIR9	Hs.406708
	215850_at 215851_at	EVI1	Hs.436019
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10	215874_at		Hs.287730 //
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	215913_s_at	CED-6	Hs.107056
		CD72	Hs.116481
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	215946_x_at	FOC91910	//
	215949_x_at	 LY9	Hs.403857
	215967_s_at	BCL6	Hs.155024
20	215990_s_at	BCL6	Hs.159901 //
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	216016_at	CIAS1	Hs.16074 //
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	216180_s_at	SYNJ2 TRD@	Hs.2014
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	216197_at	IGKV1D-13	Hs.390427
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40	216218_s_at	SLC2A14	Hs.401274
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	216320_x_at	ITGA7	Hs.74369
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	216379_x_at		//
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	216442_x_at	na TRA1	Hs.192374
	216449_x_at	TPSB2	Hs.405479
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	216511_s_at	***	//
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	216560_x_at	~~~	//
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U		FARSL	Hs.23111
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	216614_at		Hs.436196
	216620_s_at	ARHGEF1O	//
10	216667_at	IIIOGEDDA	
10	216693_x_at	HDGFRP3	Hs.127842
	216705_s_at	ADA	Hs.407135
	216733_s_at	GATM	Hs.75335
	216766_at		//
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	216833_x_at	GYPE	Hs.395535
	216834_at	RGS1	Hs.75256
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	216858_x_at		//
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	216894_x_at	CDKN1C	$\mathrm{Hs.}106070$
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	216920_s_at	TRGC2	$\mathrm{Hs.385086}$
	216925_s_at	TAL1	Hs.73828
25	216950_s_at	FCGR1A	Hs.77424
	216956_s_at	ITGA2B	Hs.411312
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	217023_x_at		//
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	217118_s_at	KIAA0930	Hs.13255
	217143_s_at	TRD@	Hs.2014
	217147_s_at	TRIM	Hs.138701
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	217157_x_at		Hs.449620 //
	217165_x_at	MT1F	Hs.438737
	217179_x_at		Hs.440830
	217192_s_at	PRDM1	$\mathrm{Hs.381140}$
40	217227_x_at		Hs.449598 //
	217232_x_at		//
	217234_s_at	VIL2	Hs.403997
	217235_x_at		Hs.449593 //
	217258_x_at		Hs.449599 //
45	217274_x_at		//
	217276_x_at	dJ222E13.1	Hs.301947
	217281_x_at		Hs.448987 //
	217284_x_at	dJ222E13.1	Hs.301947
	217286_s_at	NDRG3	Hs.437338
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	217378_x_at		//
	217388_s_at	KYNU	Hs.444471
	217404_s_at	COL2A1	Hs.408182
	217414_x_at		//
55	217418_x_at	MS4A1	Hs.438040
	217419_x_at	AGRN	Hs.273330 //
	217422_s_at	CD22	Hs.262150
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	217521_at	HAL	Hs.190783
	217521_at 217523 at	CD44	Hs.306278
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	217572_at		//
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	217655_at		Hs.407053 //
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10			Hs.499751 // est
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	217715_x_at		Hs.417310 // est
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	217736_s_at	HRI	Hs.434986
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	217762_s_at	RAB31	$\mathrm{Hs.}223025$
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	217771_at	GOLPH2	Hs.352662
	217799_x_at	UBE2H	Hs.372758
	217800_s_at	NDFIP1	Hs.9788
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	217838_s_at	EVL	Hs.241471
	217848_s_at	PP	Hs.380830
	217867_x_at	BACE2	Hs.436490
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	217911_s_at	BAG3	Hs.15259
	217941_s_at	ERBB2IP	Hs.8117
	217963_s_at	NGFRAP1	Hs.448588
	217966_s_at	Clorf24	Hs.48778
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	217977_at	SEPX1	Hs.279623
	217979_at	TM4SF13	Hs.364544
	217973_at 217983_s_at	RNASE6PL	Hs.388130
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	217988_at	HEI10	Hs.107003
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	217997_at	PHLDA1	Hs.82101
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	218000_s_at	PHLDA1	Hs.82101
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	218035_s_at	FLJ20273	Hs.95549
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	218086_at	NPDC1	Hs.105547
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	218217_at	RISC	Hs.43 1107
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	218742_at	HPRN	$\mathrm{Hs.22158}$
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		na	Hs.406494 //
	222145_at	TCF4	Hs.359289
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	222186_at	DIT D A	Hs.306329 //
	222218_s_at	PILRA	Hs.122591
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	38521_at	CD22	Hs.262150
	39248_at	AQP3	Hs.2346-42
	39318_at	TCL1A	Hs.2484
60	39402_at	IL1B	Hs.126256
	396_f_at	EPOR	Hs.1278 2 6
	39729_at	PRDX2	Hs.4321 2 1
	40020_at	CELSR3	Hs.5517 -3
	40093_at	LU	Hs.1550-48
65	40850_at	FKBP8	Hs.1734€4
	41386_i_at	KIAA0346	Hs.1039 15 //
	41469_at	PI3	Hs.1123-41
	-		

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Table 1 (continued):

	41577_at	PPP1R16B	Hs.45719
	41644_at	SASH1	Hs.166311
5	44673_at	SN	Hs.31869
	45297_at	EHD2	Hs.325650
	46665_at	SEMA4C	Hs.7188
	48031_r_at	C5orf4	Hs.10235
	48106_at	FLJ20489	Hs.438867
10	48808_at	DHFR	$\mathrm{Hs.}83765$
	49306_at	RASSF4	Hs.319124
	51158_at		Hs.27373 //
	53987_at	na	Hs.6343 //
	54037_at	HPS4	Hs.441481
15	55081_at	MIRAB13	Hs.8535
	55705_at		Hs.498224 // est
	57540_at	RBSK	Hs.11916
	57588_at	SLC24A3	Hs.439909
	64064_at	IAN4L1	Hs.412331
20	64942_at	na	Hs.7967 //
	AFFX-HUMISGF3A/M97935_5_at		//
	AFFX-HUMRGE/M10098_3_at		//
	AFFX-HUMRGE/M10098_5_at		//
	AFFX-HUMRGE/M10098_M_at		//
25	AFFX-M27830_5_at		//
	AFFX-M27830_M_at		//
	AFFX-r2-Hs18SrRNA-3_s_at		//
	AFFX-r2-Hs18SrRNA-5_at		//
	AFFX-r2-Hs18SrRNA-M_x_at		//
30	AFFX-r2-Hs28SrRNA-3_at		//
	AFFX-r2-Hs28SrRNA-M_at		//

Table 2 About 599 genes defining assigned clusters of AML as identified by

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	Affymetrix probe set id	Gene symbol	Cluster defined	Unigene ID
	202672 s_at	ATF3	cluster1	Hs.460
	201464_x_at	JUN	cluster1	Hs.78465
	202497_x_at	SLC2A3	cluster1	Hs.419240
40	204622_x_at	NR4A2	cluster1	Hs.82120
	216236_s_at	SLC2A14	cluster1	Hs.401274
	216248_s_at	NR4A2	cluster1	Hs.82120
	204621 s_at	NR4A2	cluster1	Hs.82120
	222088_s_at	SLC2A14	cluster1	Hs.401274
45	220014_at	LOC51334	cluster1	Hs.157461
	206762_at	KCNA5	cluster1	Hs.150208
	213094_at	GPR126	cluster1	Hs.419170
	218502_s_at	TRPS1	cluster1	Hs.26102
	221530_s_at	BHLHB3	cluster1	Hs.437282
50	221884_at	EVI1	cluster1	Hs.436019
	203642_s_at	KIAA0977	cluster1	$\mathrm{Hs.}300855$
	212827_at	IGHM	cluster1	Hs.153261
	205612_at	MMRN	cluster1	Hs.268107
	209200_at	MEF2C	cluster1	Hs.368950
55	214255_at	ATP10A	cluster1	Hs.125595
	201539_s_at	FHL1	cluster1	Hs.421383
	205717_x_at	PCDHGC3	cluster1	Hs.283794
	222144_at	KIF17	cluster1	Hs.130411 //
	219922_s_at	LTBP3	cluster1	Hs.289019
60	215836_s_at	PCDHGC3	cluster1	$\mathrm{Hs.}283794$
	205861_at	SPIB	cluster1	Hs.437905
	203372_s_at	SOCS2	cluster1	Hs.405946

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	209079_x_at	PCDHGC3	cluster1	Hs.283794
	215811_at		cluster1	Hs.275706 //
5	209199_s_at	MEF2C	cluster1	Hs.368950
-	207655_s_at	BLNK	cluster1	Hs.167746
	203716_s_at	DPP4	cluster1	Hs.44926
	219737_s_at		cluster1	Hs.458282 // est
	204304_s_at	PROM1	cluster1	Hs.370052
10	203373_at	SOCS2	cluster1	Hs.405946
	218237_s_at	SLC38A1	cluster1	Hs.132246
	202265_at	BMI1	cluster1	Hs.380403
	210298_x_at	FHL1	cluster1	Hs.421383
	208436_s_at	IRF7	cluster1	Hs.166120
15	210032_s_at	SPAG6	cluster1	Hs.158213
10	216652_s_at 206571_s_at	MAP4K4	cluster2	Hs.3628
	213152_s_at		cluster2	Hs.476680 // est
	214582_at	PDE3B	cluster2	Hs.337616
		HBA1	cluster2	Hs.449630
20	209458_x_at	VIL2	cluster2	Hs.403997
20	208623_s_at	HBA1	cluster2	Hs.449630
	204018_x_at	HBA1	cluster2	Hs.449630
	211745_x_at	HBB	cluster2	Hs.155376
	211696_x_at	HBA1	cluster2	Hs.449630
25	214414_x_at		cluster2	Hs.155376
20	209116_x_at	HBB	cluster2	//
	217232_x_at	HBA1	cluster2	Hs.449630
	211699_x_at		cluster2	//
	217414_x_at	CLU	cluster2	Hs.436657
30	208792_s_at		cluster2	Hs.409202
50	216268_s_at	JAG1	cluster2	Hs.182982
	208798_x_at	GOLGIN-67	cluster2 cluster2	Hs.37034
	213844_at	HOXA5		Hs.61490
	204030_s_at	SCHIP1	cluster2	Hs.81170
25	209193_at	PIM1	cluster2	Hs.433488
35	221942_s_at	GUCY1A3	cluster2	Hs.296398
	208767_s_at	LAPTM4B	cluster2	Hs.356225
	210425_x_at	GOLGIN-67	cluster2	
	209409_at	GRB10	cluster2	Hs.81875
40	212070_at	GPR56	cluster2	Hs.6527
40	205453_at	HOXB2	cluster2	Hs.290432
	208797_s_at	GOLGIN-67	cluster2	Hs.182982
	206582_s_at	GPR56	cluster2	Hs.6527
	207533_at	CCL1	cluster2	Hs.72918
4 =	206298_at	RhoGAP2	cluster2	Hs.87241
45	212276_at	LPIN1	cluster2	Hs.81412
	219615_s_at	KCNK5	cluster2	Hs.444448
	203187_at	DOCK1	cluster2	Hs.437620
	206574_s_at	PTP4A3	cluster2	Hs.43666
F0	204341_at	TRIM16	cluster2	Hs.241305
50	210145_at	PLA2G4A	cluster2	Hs.211587
	205190_at	PLS1	cluster2	Hs.203637
	215288_at	TRPC2	cluster2	Hs.131910 //
	211269_s_at	IL2RA	cluster2	Hs.130058
	206341_at	IL2RA	cluster2	Hs.130058
55	207034_s_at	GLI2	cluster2	Hs.111867
	212543_at	AIM1	cluster3	Hs.422550 //
	204500_s_at	AGTPBP1	cluster3	Hs.21542
	211729_x_at	BLVRA	cluster3	Hs.435726
	218831_s_at	FCGRT	cluster3	Hs.111903
60	221830_at	RAP2A	cluster3	Hs.48554
	203773_x_at	BLVRA	cluster3	Hs.435726
	206034_at	SERPINB8	cluster3	Hs.368077
	212195_at	IL6ST	cluster3	Hs.71968
	205707_at	IL17R	cluster3	Hs.129751
65	203973_s_at	KIAA0146	cluster3	Hs.381058
	220377_at	C14orf110	cluster3	Hs.395486
	201829_at	NET1	cluster3	Hs.25155
				

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	rabio 2 (continuada).			
	207838_x_at	PBXIP1	cluster3	Hs.8068
	201427_s_at	SEPP1	cluster3	Hs.275775
5	214228_x_at	TNFRSF4	cluster3	Hs.129780
0	201663_s_at	SMC4L1	cluster3	Hs.50758
	215388_s_at	HFL1	cluster3	Hs.296941
	203187_at	DOCK1	cluster3	Hs.437620
	219304_s_at	SCDGF-B	cluster3	Hs.112885
10	219602_s_at	FLJ23403	cluster3	Hs.293907
10	215471_s_at	MAP7	cluster3	Hs.254605
	202890_at	MAP7	cluster3	Hs.254605
	206582_s_at	GPR56	cluster3	Hs.6527
	214039 s_at	LAPTM4B	cluster3	Hs.296398
15	204341_at	TRIM16	cluster3	Hs.241305
	204160 s at	ENPP4	cluster3	Hs.54037
	213217_at	ADCY2	cluster3	Hs.414591
	210116_at	SH2D1A	cluster3	Hs.151544
	201664_at	SMC4L1	cluster3	Hs.50758
20	217975_at	LOC51186	cluster3	Hs.15984
	202889_x_at	ANPEP	cluster3	Hs.254605
	204044_at	QPRT	cluster3	Hs.8935
	208029_s_at	LAPTM4B	cluster3	Hs.296398
	206298_at	RhoGAP2	cluster3	Hs.87241
25	208767_s_at	LAPTM4B	cluster3	Hs.296398
	213110_s_at	COL4A5	cluster3	Hs.169825
	205190_at	PLS1	cluster3	Hs.203637
	207533_at	CCL1	cluster3	Hs.72918
	205848_at	GAS2	cluster3	Hs.135665
30	206950_at	SCN9A	cluster3	Hs.2319
	210844_x_at	CTNNA1	cluster4	Hs.254321
	200764_s_at	CTNNA1	cluster4	Hs.254321
	200765_x_at	CTNNA1	cluster4	Hs.254321
~ =	209191_at	TUBB-5	cluster4	Hs.274398
35	202241_at	C8FW	cluster4	Hs.444947
	217800_s_at	NDFIP1	cluster4	Hs.9788
	202252_at	RAB13	cluster4	Hs.151536
	201412_at	LRP10	cluster4	Hs.28368
40	201160_s_at	CSDA	cluster4	Hs.221889
40	208683_at	CAPN2	cluster4	Hs.350899
	205382_s_at	DF	cluster4	Hs.155597
	203233_at	IL4R	cluster4	Hs.75545
	219371_s_at	KLF2	cluster4	Hs.107740
4	208923_at	CYFIP1	cluster4	Hs.26704
45	218627_at	FLJ11259	cluster4	Hs.416393
	213416_at	ITGA4	cluster4	Hs.145140
	205884_at	ITGA4	cluster4	Hs.145140
	214757_at		cluster4	Hs.488749 // est Hs.114218
50	203987_at	FZD6	cluster4	Hs.439586
50	202242_at	TM4SF2	cluster4	Hs.128433
	206726_at	PGDS	cluster4	Hs.441481
	54037_at	HPS4	cluster4	Hs.278467
	216525_x_at	PMS2L9	cluster4 cluster4	Hs.408615
55	210448_s_at	P2RX5 ABCB1	cluster4	Hs.21330
JJ	209993_at		cluster4	Hs.138701
	217147_s_at	TRIM B4GALT6	cluster4	Hs.369994
	206233_at	ABCB1	cluster4	Hs.21330
	209994_s_at 220567_at	ZNFN1A2	cluster4	Hs.278963
60		C18orf1	cluster4	Hs.285091
00	207996_s_at 213910_at	IGFBP7	cluster4	Hs.435795
	213910_at 214049_x_at	CD7	cluster4	Hs.36972
	214545_x_at 214551_s_at	CD7	cluster4	Hs.36972
	214551_s_at 217143_s_at	TRD@	cluster4	Hs.2014
65	219383_at	FLJ14213	cluster4	Hs.183506
- -	211682_x_at	UGT2B28	cluster4	Hs.137585
	213830_at	TRD@	cluster4	Hs.2014
	· 	_		

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	900999 - 04	B4GALT6	cluster4	Hs.369994
	206232_s_at	TRD@	cluster4	Hs.2014
5	216191_s_at		cluster4	Hs.306324 //
J	216286_at	TFEB	cluster5	Hs.23391
	50221_at	EPHB4	cluster5	Hs.156114
	202895_s_at	CCR1	cluster5	Hs.301921
	205099_s_at	PSAP	cluster5	Hs.406455
10	200866_s_at	LILRB3	cluster5	Hs.306230
10	208594_x_at	LILRB3	cluster5	Hs.306230
	211135_x_at	ASM3A	cluster5	Hs.277962
	213624_at	MAFB	cluster5	Hs.169487
	218559_s_at	RASSF4	cluster5	Hs.319124
15	221578_at 212334_at	GNS	cluster5	Hs.334534
10	—	STS	cluster5	Hs.79876
	203769_s_at	CD86	cluster5	Hs.27954
	205686_s_at 205685_at	CD86	cluster5	Hs.27954
	_	LILRB1	cluster5	Hs.149924
20	207104_x_at	CARD15	cluster5	Hs.135201
20	220066_at	IFNGR2	cluster5	Hs.409200
	201642_at	KCNQ1	cluster5	Hs.367809
	204487_s_at	MGC4342	cluster5	Hs.301342
	217992_s_at	HNMT	cluster5	Hs.42151
25	211732_x_at	LILRB1	cluster5	Hs.149924
20	210660_at	ECGF1	cluster5	Hs.435067
	204858_s_at	STS	cluster5	Hs.79876
	203768_s_at	PILRA	cluster5	Hs.122591
	222218_s_at	LILRB3	cluster5	Hs.306230
30	210146_x_at	TLR8	cluster5	Hs.272410
30	220832_at	PHT2	cluster5	Hs.237856
	219593_at	CSPG2	cluster5	Hs.434488
	204619_s_at	PTAFR	cluster5	Hs.46
	206278_at	SIGLEC7	cluster5	Hs.274470
35	207224_s_at	STS	cluster5	Hs.79876
50	203767_s_at	VDR	cluster5	Hs.2062
	204254_s_at	UBE2D1	cluster5	Hs.129683
	214590_s_at	EPB41L3	cluster5	Hs.103839
	212681_at	DKFZp434L142	cluster5	Hs.323583
40	219872_at	CAMK1	cluster5	Hs.434875
40	204392_at	PILRA	cluster5	Hs.122591
	219788_at	SIRPB1	cluster5	Hs.194784
	206934_at	EPB41L3	cluster5	Hs.103839
	211776_s_at	LILRB1	cluster5	Hs.149924
45	207872_s_at 206710_s_at	EPB41L3	cluster5	Hs.103839
40	209083_at	CORO1A	cluster6	Hs.415067
	204319_s_at	RGS10	cluster6	Hs.82280
	204315_s_at 217845_x_at	HIG1	cluster6	Hs.7917
	205672_at	XPA	cluster6	Hs.288867
50	217118_s_at	KIAA0930	cluster6	Hs.13255
90	217116_s_at 211990_at	HLA-DPA1	cluster6	Hs.914
	210982_s_at	HLA-DRA	cluster6	Hs.409805
	208982_at	PECAM1	cluster6	Hs.78146
	209619_at	CD74	cluster6	Hs.446471
55	215193_x_at	HLA-DRB1	cluster6	Hs.411726
00	201641_at	BST2	cluster6	Hs.118110
	213266_at		cluster6	Hs.497941 // est
	202729_s_at	LTBP1	cluster6	Hs.241257
	204751_x_at	DSC2	cluster6	Hs.95612
60	215573_at	CAT	cluster6	Hs.395771
00	220898 at		cluster6	//
	215388_s_at	HFL1	cluster6	Hs.296941
	219036_s_at	BITE	cluster6	Hs.127217
	204750 sat	DSC2	cluster6	Hs.95612
65	218786_at		cluster6	Hs.374350
	208414_s_at	HOXB4	cluster6	Hs.147465
	201431_s_at	DPYSL3	cluster6	Hs.150358

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	04 #000	CMCAT 1	alakawC	Hs.50758
	215623_x_at	SMC4L1	cluster6	Hs.348883
5	213260_at	FOXC1	cluster6	Hs.49765
Θ	219932_at	VLCS-H1	cluster6	Hs.44481
	206377_at	FOXF2	cluster6	Hs.241257
	202728_s_at	LTBP1	cluster6	Hs.317659
	219651_at	FLJ10713	cluster6	Hs.414591
10	213217_at	ADCY2	cluster6	
10	218710_at	FLJ20272	cluster6	Hs.26090
	219602_s_at	FLJ23403	cluster6	Hs.293907
	215807_s_at	PLXNB1	cluster6	Hs.278311
	212019_at	DKFZP564M182	cluster6	Hs.158995
	204983_s_at	GPC4	cluster6	Hs.58367
15	204984_at	GPC4	cluster6	Hs.58367
	221959_at	MGC39325	cluster6	Hs.34054
	209702_at	FTO	cluster6	Hs.284741
	219511_s_at	SNCAIP	cluster6	Hs.24948
	51158_at		cluster6	Hs.27373 //
20	221880_s_at		cluster6	Hs.27373 //
	201733_at	CLCN3	cluster7	Hs.372528
	218978_s_at	MSCP	cluster7	Hs.283716
	214433_s_at	SELENBP1	cluster7	Hs.334841
	201249_at	SLC2A1	cluster7	Hs.169902
25	205389_s_at	ANK1	cluster7	Hs.443711
	207793_s_at	EPB41	cluster7	Hs.37427
	212804_s_at	DKFZP434C212	cluster7	Hs.287266
	221237_s_at	OSBP2	cluster7	Hs.7740
	216925_s_at	TAL1	cluster7	Hs.73828
30	206077_at	KEL	cluster7	Hs.420322
00	213843_x_at	SLC6A8	cluster7	Hs.388375
	206145_at	RHAG	cluster7	Hs.368178
	217274_x_at		cluster7	//
	217274_A_at 216063_at		cluster7	Hs.470084 // est
35	220751_s_at	C5orf4	cluster7	Hs.10235
00	210854_x_at	SLC6A8	cluster7	Hs.388375
	210594_x_at 210586_x_at	RHD	cluster7	Hs.458333
		MYL4	cluster7	Hs.356717
	210395_x_at	KCNH2	cluster7	Hs.188021
40	205262_at	ANK1	cluster7	Hs.443711
40	208353_x_at	SPTB	cluster7	Hs.438514
	208416_s_at		cluster7	Hs.431099
	219630_at	MAP17	cluster7	Hs.443711
	208352_x_at	ANK1		Hs.443711
45	207087_x_at	ANK1	cluster7	Hs.368178
45	211254_x_at	RHAG	cluster7	
	206647_at	HBZ	cluster7	Hs.272003
	214530_x_at	EPB41	cluster7	Hs.37427
	203911_at	RAP1GA1	cluster7	Hs.433797
F0	218864_at	TNS	cluster7	Hs.439442
50	207043_s_at	SLC6A9	cluster7	Hs.442590
	205391_x_at	ANK1	cluster7	Hs.443711
	210088_x_at	MYL4	cluster7	Hs.356717
	216054_x_at	MYL4	cluster7	Hs.356717
	206146_s_at	\mathbf{RHAG}	cluster7	Hs.368178
55	204720_s_at	DNAJC6	cluster7	Hs.44896
	205390_s_at	ANK1	cluster7	Hs.443711
	56748_at	TRIM10	cluster7	$\mathbf{Hs.274295}$
	221577_x_at	PLAB	cluster7	Hs.296638
	207854_at	GYPE	cluster7	$\mathrm{Hs.395535}$
60	206116_s_at	TPM1	cluster7	Hs.133892
	203115_at	FECH	cluster8	Hs.443610
	208352_x_at	ANK1	cluster8	Hs.443711
	48031_r_at	C5orf4	cluster8	Hs.10235
	214433_s_at	SELENBP1	cluster8	Hs.334841
65	218853_s_at	DJ473B4	cluster8	Hs.57549
00	209890_at	TM4SF9	cluster8	Hs.8037
	209890_at 210586_x_at	RHD	cluster8	Hs.458333
	_10005_n_a0			·

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	213843_x_at	SLC6A8	cluster8	Hs.388375
	207087_x_at	ANK1	cluster8	Hs.443711
5	204467_s_at	SNCA	cluster8	Hs.76930
O	216317_x_at	RHCE	cluster8	Hs.278994
	202124_s_at	ALS2CR3	cluster8	Hs.154248
	216833_x_at	GYPE	cluster8	Hs.395535
	201886_at	WDR23	cluster8	Hs.283976
10	202074 s at	OPTN	cluster8	Hs.390162
10	215812_s_at		cluster8	Hs.499113 // est
	218864_at	TNS	cluster8	Hs.439442
	211820_x_at	GYPA	cluster8	Hs.34287
	203794_at	CDC42BPA	cluster8	Hs.18586
15	216925_s_at	TAL1	cluster8	Hs.73828
1.0	202219_at	SLC6A8	cluster8	Hs.388375
	205838_at	GYPA	cluster8	Hs.34287
	211649_x_at		cluster8	Hs.449057
	217572_at		cluster8	//
20	202125_s_at	ALS2CR3	cluster8	Hs.154248
	208353_x_at	ANK1	cluster8	Hs.443711
	205837_s_at	GYPA	cluster8	Hs.34287
	202364_at	MXI1	cluster8	Hs.118630
	220751_s_at	C5orf4	cluster8	$\mathrm{Hs.}10235$
25	214464_at	CDC42BPA	cluster8	Hs.18586
	221237_s_at	OSBP2	cluster8	Hs.7740
	205391_x_at	ANK1	cluster8	Hs.443711
	210430_x_at	RHD	cluster8	Hs.283822
	201333_s_at	ARHGEF12	cluster8	Hs.413112
30	212151_at	PBX1	cluster8	Hs.408222
	40093_at	LU	cluster8	Hs.155048
	202073_at	OPTN	cluster8	Hs.390162
	209735_at	ABCG2	cluster8	Hs.194720
	201131_s_at	CDH1	cluster8	Hs.194657
35	213338_at	RIS1	cluster8	Hs.35861
	200675_at	CD81	cluster9	Hs.54457
	202370_s_at	CBFB	cluster9	Hs.179881
	211031_s_at	CYLN2	cluster9	Hs.104717
	218927_s_at	CHST12	cluster9	Hs.25204
40	206788_s_at	CBFB	cluster9	Hs.179881
	219218_at	FLJ23058	cluster9	Hs.415799
	211026_s_at	\mathbf{MGLL}	cluster9	Hs.409826
	204198_s_at	RUNX3	cluster9	Hs.170019
	213779_at	EMU1	cluster9	Hs.289106
45	218414_s_at	NDE1	cluster9	Hs.263925
	200984_s_at	CD59	cluster9	Hs.278573
	204197_s_at	RUNX3	cluster9	Hs.170019
	203329_at	PTPRM	cluster9	Hs.154151
~	218876_at	CGI-38	cluster9	Hs.412685
50	210889_s_at	FCGR2B	cluster9	Hs.126384
	212771_at	LOC221061	cluster9	Hs.66762 //
	202481_at	SDR1	cluster9	Hs.17144
	205330_at	MN1	cluster9	Hs.268515
==	203939_at	NT5E	cluster9	Hs.153952 Hs.301664
55	212912_at	RPS6KA2	cluster9	Hs.421496
	201506_at	TGFBI	cluster9	Hs.111779
	200665_s_at	SPARC	cluster9	Hs.8904
	204787_at	Z39IG	cluster9 cluster9	Hs.435625
60	207194_s_at	ICAM4	cluster9	Hs.18268
00	219308_s_at	AK5 CHI3L1	cluster9	Hs.382202
	209395_at		cluster9	Hs.425144
	205076_s_at	CRA FLJ11127	cluster9	Hs.91165
	219694_at	CHI3L1	cluster9	Hs.382202
65	209396_s_at	MSLN	cluster9	Hs.408488
UU	204885_s_at 221019_s_at	COLEC12	cluster9	Hs.29423
	221019_s_at 205987_at	CD1C	cluster9	Hs.1311
	200001_av	0010	STADUCTO	

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	,			
	203058 s_at	PAPSS2	cluster9	Hs.274230
	203060_s_at	PAPSS2	cluster9	Hs.274230
5	206682_at	CLECSF13	cluster9	Hs.54403
J	212298_at	NRP1	cluster9	Hs.173548
	206135_at	ST18	cluster9	Hs.151449
	212358_at	CLIPR-59	cluster9	Hs.7357
	207961_x_at	MYH11	cluster9	Hs.78344
10	201497_x_at	MYH11	cluster9	Hs.78344
	214575_s_at	AZU1	cluster10	Hs.72885
	205382_s_at	DF	cluster10	Hs.155597
	209906_at	C3AR1	cluster10	Hs.155935
	206111_at	RNASE2	cluster10	Hs.728
15	212071_s_at	SPTBN1	cluster10	Hs.205401
	203796_s_at	BCL7A	cluster10	$\mathrm{Hs.371758}$
	218899_s_at	BAALC	cluster10	Hs.169395
	209488_s_at	RBPMS	cluster10	Hs.195825
	218086_at	NPDC1	cluster10	Hs.105547
20	204581_at	CD22	cluster10	Hs.262150
	208614_s_at	FLNB	cluster10	Hs.81008
	204540_at	EEF1A2	cluster10	Hs.433839
	204917_s_at	MLLT3	cluster10	Hs.404
	209437_s_at	SPON1	cluster10	Hs.5378
25	212827_at	IGHM	cluster10	Hs.153261
	200672_x_at	SPTBN1	cluster10	Hs.205401
	203756_at	P164RHOGEF	cluster10	Hs.45180
	220377_at	C14orf110	cluster10	Hs.395486
	209576_at	GNAI1	cluster10	Hs.203862
30	205330_at	MN1	cluster10	Hs.268515
	212750_at	PPP1R16B	cluster10	Hs.45719
	204484_at	PIK3C2B	cluster10	Hs.343329
	209436_at	SPON1	cluster10	Hs.5378
	209282_at	PRKD2	cluster10	Hs.205431
35	207836_s_at	RBPMS	cluster10	Hs.195825
	209487_at	RBPMS	cluster10	$\mathrm{Hs.}195825$
	204083_s_at	TPM2	cluster10	Hs.300772
	207788_s_at	SCAM-1	cluster10	Hs.301302
	212558_at	GDAP1L1	cluster10	Hs.20977
40	209679_s_at	LOC57228	cluster10	${ m Hs.206501}$
	41577_at	PPP1R16B	cluster10	Hs.45719
	213506_at	F2RL1	cluster10	Hs.154299
	205933_at	SETBP1	cluster10	Hs.201369
	204004_at		cluster10	Hs.503576 // est
45	213488_at	FLJ00133	cluster10	Hs.7949
	200671_s_at	SPTBN1	cluster10	Hs.205401
	209763_at	NRLN1	cluster10	$\mathrm{Hs.440324}$
	47560_at	FLJ11939	cluster10	Hs.94229
	202551_s_at	CRIM1	cluster10	$\mathrm{Hs.}170752$
50	219145_at	FLJ11939	cluster10	Hs.94229
	201560_at	CLIC4	cluster11	Hs.25035
	204401_at	KCNN4	cluster11	Hs.10082
	212658_at	LHFPL2	cluster11	Hs.79299
	221223_x_at	CISH	cluster11	Hs.8257
55	201559_s_at	CLIC4	cluster11	Hs.25035
	201425_at	ALDH2	cluster11	Hs.436437
	209543_s_at	CD34	cluster11	Hs.374990
	203217_s_at	SIAT9	cluster11	Hs.415117
0.0	215116_s_at	DNM1	cluster11	Hs.436132
60	213848_at	DUSP7	cluster11	Hs.3843
	200665_s_at	SPARC	cluster11	Hs.111779
	211675_s_at	HIC	cluster11	Hs.132739
	208873_s_at	DP1	cluster11	Hs.173119
a =	205101_at	MHC2TA	cluster11	Hs.126714
65	209723_at	SERPINB9	cluster11	Hs.104879
	200762_at	DPYSL2	cluster11	Hs.173381
	201279_s_at	DAB2	cluster11	Hs.81988

Table 2 (continued):

	Table 2 (continued).			
	217838_s_at	EVL	cluster11	Hs.241471
	218589_at	P2RY5	cluster11	Hs.123464
5	216033_s_at	FYN	cluster11	Hs.390567
Ü	218966_at	MYO5C	cluster11	Hs.111782
	31874_at	GAS2L1	cluster11	Hs.322852
	203139_at	DAPK1	cluster11	Hs.244318
	208886_at	H1F0	cluster11	Hs.226117
10	201656_at	ITGA6	cluster11	Hs.212296
	219777_at	hIAN2	cluster11	Hs.105468
	218237_s_at	SLC38A1	cluster11	Hs.132246
	212171_x_at	VEGF	cluster11	Hs.73793
	203542_s_at	BTEB1	cluster11	$\mathrm{Hs.150557}$
15	203859_s_at	PALM	cluster11	Hs.78482
	214953_s_at	APP	cluster11	Hs.177486
	2188 05_ at	IAN4L1	cluster11	Hs.412331
	204385_at	KYNU	cluster11	Hs.444471
	209583_s_at	MOX2	cluster11	Hs.79015
20	206042_x_at	SNRPN	cluster11	Hs.48375
	201601_x_at	IFITM1	cluster11	Hs.458414
	201522_x_at	SNRPN	cluster11	Hs.48375
	218825_at	EGFL7	cluster11	Hs.91481
05	207076_s_at	ASS	cluster11	Hs.160786
25	209079_x_at	PCDHGC3	cluster11	Hs.283794 Hs.3109
	204425_at	ARHGAP4	cluster12 cluster12	Hs.81337
	203236_s_at	LGALS9 MFNG	cluster12 cluster12	Hs.371768
	204152_s_at	NRIP1	cluster12 cluster12	Hs.155017
30	202600_s_at 204362_at	SCAP2	cluster12	Hs.410745
50	200931_s_at	VCL	cluster12	Hs.75350
	202599_s_at	NRIP1	cluster12	Hs.155017
	204153_s_at	MFNG	cluster12	Hs.371768
	200935_at	CALR	cluster12	Hs.353170
35	210140_at	CST7	cluster12	Hs.143212
	200656_s_at	P4HB	cluster12	Hs.410578
	200654_at	P4HB	cluster12	Hs.410578
	214203_s_at	PRODH	cluster12	Hs.343874
4.0	206105_at	FMR2	cluster12	Hs.54472
40	211663_x_at	PTGDS	cluster12	Hs.446429
	207031_at	BAPX1	cluster12	Hs.105941
	212204_at	DKFZP564G2022	cluster12	Hs.200692
	200770_s_at	LAMC1	cluster12	Hs.432855
45	209960_at	HGF	cluster12	Hs.396530 Hs.159360
45	207650_x_at	PTGER1	cluster12 cluster12	Hs.356623 // est
	212509_s_at	RAB5B	cluster12 cluster12	Hs.77690
	201276_at 209815_at	na	cluster12	Hs.454253 //
	209961_s_at	HGF	cluster12	Hs.396530
50	218043_s_at	AZ2	cluster12	Hs.437336
00	207895_at	NAALADASEL	cluster12	Hs.13967
	212732_at	MEG3	cluster12	Hs.418271
	203397_s_at	GALNT3	cluster12	Hs.278611
	210755_at	HGF	cluster12	Hs.396530
55	206634_at	SIX3	cluster12	Hs.227277
	203074_at	ANXA8	cluster12	Hs.87268
	216320_x_at	MST1	cluster12	Hs.349110
	202260_s_at	STXBP1	cluster12	Hs.325862
	205663_at	PCBP3	cluster12	Hs.121241
60	205614_x_at	MST1	cluster12	Hs.349110
	204537_s_at	GABRE	cluster12	Hs.22785
	210794_s_at	MEG3	cluster12	Hs.418271
	205110_s_at	FGF13	cluster12	Hs.6540 Hs.396530
65	210998_s_at	HGF HGF	cluster12 cluster12	Hs.396530
UU	210997_at	WBSCR5	cluster12 cluster13	Hs.56607
	221581_s_at 220560_at	C11orf21	cluster13	Hs.272100
	ZZVOOU_AL	01101121	CIADIOI IO	220.2

Table 2 (continued):

	` ,			
	208091_s_at	DKFZP564K0822	cluster13	Hs.4750
	204494_s_at	LOC56905	cluster13	Hs.306331
5	208885_at	LCP1	cluster13	Hs.381099
	203741_s_at	ADCY7	cluster13	Hs.172199
	210010_s_at	SLC25A1	cluster13	Hs.111024
	214946_x_at	FLJ10824	cluster13	Hs.375174 //
	211685_s_at	NCALD	cluster13	Hs.90063
10	206793_at	PNMT	cluster13	Hs.1892
	209822_s_at	VLDLR	cluster13	Hs.370422
	204073_s_at	C11orf9	cluster13	Hs.184640
	219686_at	HSA250839	cluster13	$\mathrm{Hs.58241}$
	214920_at	LOC221981	cluster13	Hs.23799 //
15	218742_at	HPRN	cluster13	Hs.22158
	201655_s_at	HSPG2	cluster13	Hs.211573
	204396_s_at	GPRK5	cluster13	Hs.211569
	203088_at	FBLN5	cluster13	Hs.11494
	213894_at	LOC221981	cluster13	Hs.23799 //
20	201621_at	NBL1	cluster13	Hs.439671
	216356_x_at	BAIAP3	cluster13	Hs.458427
	206622_at	TRH	cluster13	Hs.182231
	218613_at	DKFZp761K1423	cluster13	Hs.236438
~ =	212492_s_at	KIAA0876	cluster13	Hs.301011 //
25	212496_s_at	KIAA0876	cluster13	Hs.301011 //
	203065_s_at	CAV1	cluster13	Hs.74034
	204874_x_at	BAIAP3	cluster13	Hs.458427
	206128_at	ADRA2C	cluster13	Hs.123022
00	216832_at	CBFA2T1	cluster13	Hs.90858
30	212097_at	CAV1	cluster13	Hs.74034
	204990_s_at	ITGB4	cluster13	Hs.85266
	211341_at	POU4F1	cluster13	Hs.458303
	211517_s_at	IL5RA	cluster13	Hs.68876
25	210744_s_at	IL5RA	cluster13	Hs.68876
35	206940_s_at	POU4F1	cluster13	Hs.458303
	204811_s_at	CACNA2D2	cluster13	Hs.389415 Hs.301198
	213194_at	ROBO1	cluster13	Hs.90858
	216831_s_at	CBFA2T1 CBFA2T1	cluster13 cluster13	Hs.90858
40	205528_s_at	CBFA2T1	cluster13	Hs.90858
40	205529_s_at	GNA12	cluster 15	Hs.182874
	221737_at	DRPLA	cluster 15	Hs.169488
	40489_at 218501_at	ARHGEF3	cluster15	Hs.25951
	217853_at	TEM6	cluster15	Hs.12210
45	220974_x_at	BA108L7.2	cluster15	Hs.283844
10	209191_at	TUBB-5	cluster15	Hs.274398
	212459_x_at	SUCLG2	cluster15	Hs.446476
	212311_at	KIAA0746	cluster 15	Hs.49500 //
	218847_at	IMP-2	cluster15	Hs.30299
50	215772_x_at	SUCLG2	cluster15	Hs.247309 //
	212314_at	KIAA0746	cluster15	Hs.49500 //
	202236_s_at	SLC16A1	cluster15	Hs.75231
	201841_s_at	HSPB1	cluster15	Hs.76067
	217800_s_at	NDFIP1	cluster15	Hs.9788
55	217226_s_at	PMX1	cluster15	Hs.443452
	202391_at	BASP1	cluster15	Hs.79516
	200765_x_at	CTNNA1	cluster15	Hs.254321
	213400_s_at	TBL1X	cluster15	Hs.76536
	213147_at	HOXA10	cluster15	Hs.110637
60	212906_at	na	cluster15	Hs.347534 //
	218552_at	FLJ10948	cluster15	Hs.170915
	214651_s_at	HOXA9	cluster15	Hs.127428
	210365_at	RUNX1	cluster15	Hs.410774
a=	209374_s_at	IGHM	cluster15	Hs.153261
65	213150_at	HOXA10	cluster15	Hs.110637
	201719_s_at	EPB41L2	cluster15	Hs.440387
	218627_at	FLJ11259	cluster15	Hs.416393

Table 2 (continued):

	rabio 2 (continuou).			
	219256_s_at	FLJ20356	cluster15	Hs.61053
	205453_at	HOXB2	cluster15	Hs.290432
5	208962_s_at	FADS1	cluster15	Hs.132898
U	205600_x_at	HOXB5	cluster15	Hs.149548
		MEIS1	cluster 15	Hs.170177
	204069_at	TBL1X	cluster15	Hs.76536
	201867_s_at		cluster15	Hs.127428
10	209905_at	HOXA9		Hs.446476
TO	214835_s_at	SUCLG2	cluster15	Hs.150557
	203542_s_at	BTEB1	cluster15	
	212827_at	IGHM	cluster15	Hs.153261
	211182_x_at	RUNX1	cluster15	Hs.410774
- F	204661_at	CDW52	cluster15	Hs.276770
15	206676_at	CEACAM8	cluster15	Hs.41
	220057_at	GAGED2	cluster16	Hs.112208
	219360_s_at	TRPM4	cluster16	Hs.31608
	219414_at	CLSTN2	cluster16	Hs.12079
00	220116_at	KCNN2	cluster16	Hs.98280
20	216370_s_at	TKTL1	cluster16	Hs.102866
	205550_s_at	BRE	cluster16	Hs.80426
	211566_x_at	BRE	cluster16	Hs.80426
	214183_s_at	TKTL1	cluster16	Hs.102866
~~	209031_at	IGSF4	cluster16	Hs.156682
25	212645_x_at	BRE	cluster16	Hs.80426
	209030_s_at	IGSF4	cluster16	Hs.156682
	213791_at	PENK	cluster16	Hs.339831
	206508_at	TNFSF7	cluster16	Hs.99899
00	219506_at	FLJ23221	cluster16	Hs.91283
30	211421_s_at	RET	cluster16	Hs.350321
	203241_at	UVRAG	cluster16	Hs.13137
	213908_at	LOC339005	cluster16	Hs.212670 //
	207911_s_at	TGM5	cluster16	Hs.129719
0.5	214190_x_at	GGA2	cluster16	Hs.133340
35	204561_x_at	APOC2	cluster16	Hs.75615
	209663_s_at	ITGA7	cluster16	Hs.74369 Hs.6980
	214259_s_at	AKR7A2	cluster16	
	205472_s_at	DACH	cluster16	Hs.63931
40	216331_at	ITGA7	cluster16	Hs.74369
40	220010_at	KCNE1L	cluster16	Hs.146372
	213484_at	na	cluster16	Hs.66187 // Hs.20196
	204497_at	ADCY9	cluster16	
	215771_x_at	RET	cluster16	Hs.350321
4 5	209032_s_at	IGSF4	cluster16	Hs.156682 Hs.435112
45	219714_s_at	CACNA2D3	cluster16	Hs.22920
	219463_at	C20orf103	cluster16	Hs.6980
	202139_at	AKR7A2	cluster16	Hs.8562
	219143_s_at	FLJ20374	cluster16	Hs.294008
EΩ	205996_s_at	AK2	cluster16	Hs.47166
50	219288_at	HT021	cluster16	Hs.28578
	215663_at	MBNL1	cluster16	Hs.416543
	213361_at	PCTAIRE2BP	cluster16	Hs.133340
	210658_s_at	GGA2	cluster16	Hs.133340
55	213772_s_at	GGA2 AK2	cluster16 cluster16	Hs.294008
ออ	212174_at	ANZ	Cluster 10	113.204000

Table 3

	Abnormality	10-fold CV error	Error validation set	#Probe sets	#Genes
	t(8;21) - AML1/ETO	0/190	0/96	3	2
5	t(15;17) - $PML/RAR\alpha$	1/190	0/96	3	2
	inv(16) - CBFβ/MYH11	0/190	0/96	1	1
	11q23 (cluster #16)	3/190	3/96	31	25
	EVI1 (cluster #10)	16/190	0/96	28	25
	$cEBP\alpha$ (cluster #4)	8/190	2/96	13	8
10	cEBPlpha (cluster #15)	17/190	6/96*	36	32
	cEBPlpha (cluster #4 and #15)	5/190	2/96	9	5
	FLT3 ITD	27/190	21/96	56	41

Table 4. Clinical and molecular characteristics of the 286 patients with de novo AML.

5	Gender Male Female		# 138 148	% 49 51
10	Age groups Younger than 35 35-60 60 and older		77 177 32	27 62 11
	Age (median (range)		45.1 (15.2-77.6)	
15	White blood cell (WBC) count (109/l, median (range))		75,5 (0.3-263)	
	Blast count (%, median (range))		70 (0-98)	
20	Platelet count (109/l, median (range))		57 (3-931)	
	FAB M0 M1	6 64	2 22 23	
25	M2 M3 M4 M5	66 19 53 65	25 7 18 23	
30	M6 Mixed Unclassified	3 8 2	1 3 1	
00	Cytogenetic risk groups Favourable	58	20	
35	t(8;21) inv(16) t(15;17) Unfayourable	22 19 17 39	$egin{array}{c} 8 \\ 7 \\ 6 \\ 14 \end{array}$	
40	11q23 abnormalities -5/7(q) abnormalities Normal Cytogenetics	17 22 118	6 8 41	
	Molecular abnormalities Mutation			
45	FLT3 ITD FLT3 TKD N-RAS K-RAS	78 33 26 9	$egin{array}{c} 27 \\ 12 \\ 9 \\ 3 \end{array}$	
50	cEBPlpha Overexpression EVI1	17 24	6 8	

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Table 5.

	#Probe sets:	147	293	569	984	1692	2856	5071
E	Ratio:	>32	>22.6	>16	>11.3	>8	>5.6	>4
5	chromosomal abno	rmalities						
	t(8;21)	+/-	+	+	+	++	++	+
	inv(16)	+/-	+/-	+/-	+	++	++	++
	t(15;17)	+/-	+	++	++	++	++	+
10	11q23	+/-	+/-	+/-	+/-	+	+	+/-
	-7(q)	+/-	+/-	+/-	+/-	+/-	+	+/-
	mutation							
	FLT3 ITD	+/-	+/-	+/-	+/-	+/-	+/-	+/-
15	FLT3 TKD	-	-	-	-	-	-	-
	N-RAS	-	-	-	-	-	-	-
	K- RAS	-	-	-	-	-	-	-
	cEBPlpha	-	+/-	+/-	+	+	+	+
20	overexpression							
	EVI1	_	_	_	-	+/-	+	+/-

^{(++: 100%} clustering, +: clustering in \leq 2 recognizable clusters, +/-: clustering in \geq 2 recognizable clusters, - : no clustering)

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase Table 6: Characteristics of cluster #1 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$ mutation in CEBPA, ND: not determined).

rO

	Patient	Cluster	FAB		FLT3 ITD	FLT3 TKD	N-RAS K-RAS	K-RAS	EVII	CEBPA
	1595	#1	M1	NN	+		•		•	1
10	2187	#1	M1	NN				ı	1	1
	3488	#1	M1	Complex			•	ı	•	1
	1401	#1	M1	NN	•	1		1	•	1
	2255	#1	M1	11q23(t(4;11))	•	1	•	+	•	1
	2302	#1	M1	+11/11q23(sMLL)		t	,	1	,	ı
15	2765	#1	M1	+11/+11/Other	1	t	ij.	ı		t
	2280	#1	M2	NN	,	1	ı	1		1
	3304	#1	M5	NN	+	ı	•	1	ı	•
	3328	#1	M5	11q23 (t(11;19))	ı	ı		ı	+	ı
	2682	#1	M4	Other/11q23 $(t(2;9;11))$	· (ı		ı	+	1
20	2207	#1	M1	11q23 (t(6;11))	ı	ı		1	+	1
	2772	#1	M5	11q23 (t(6;11))	1	1		1	+	
	2196	#1	M5	NN		1		1	+	1

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase Table 7: Characteristics of cluster #2 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$ mutation in CEBPA, ND: not determined).

CEBPA																	
EVII	ı			ı	1	ı	•	•	1	1	1	•					1
K- RAS	,		ı	1	,	•		•	•	t	•	t		•	ı	•	1
N-RAS	1	ı	,	ı	•	1	,	,	ı					1	t		1
FLT3 TKD																	
$FLT3~\mathrm{ITD}$	1	+	+	ı	ı	+	+	+	+	+	+	+	+	+	+	+	+
Karyotype	8+	NN	NN	-9q	NN	t(6;9)	NN	8+									
FAB	M4	M1	R	M4	M4	M4	M4	M5	M5	M1	M5	M4	M2	M4	M1	M4	M5
Cluster	#5	#5	#5	#2	#5	#2	#5	#2	#5	#5	#5	#5	#5	#5	#5	#5	#2
Patient	3330	2681	2688	2685	2689	2498	2183	2214	2201	3100	2672	2195	1747	2774	1551	2194	2182
		10					15					20					25

+

R

M2

#3

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase Table 8: Characteristics of cluster #3 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$ mutation in CEBPA, ND: not determined). 20

#3 M1 NN + -	Patient	Clu	FAB	Karyotype	FLT3 ITD	$FLT3~\mathrm{TKD}$	N- RAS	K- RAS	EVII	CEBPA
M2 NN + -		#3	M1	N	+	1	,	t	ı	ı
M1 NN + -		#3	M2	NN	+	1	1	1	ì	•
M2 NN + -		#3	M1	NN	+	•	ı		1	
M2 NN + -		#3	M2	NN	+	t	1	1	ı	ı
M1 NN -		#3	M2	NN	+	,	•	ı	ı	
M1 NN + -		#3	M1	NN	•	ı	•	ĭ		
M1 NN + -		#3	M1	NN	+	ī	•	ı	•	•
M1 NN + - - + - + - + + - + + + + + + + + - + - + - - + -		#3	M1	NN	+	•	1	ı		ı
M2 t(9;22) - + - + - + - - + -<		#3	M1	NN	+	1		•		
M1 +8/Other - + -		#3	M2	t(9;22)	1	ı		•	+	
M4 NN -		#3	M1	+8/Other	•	+		1		1
M4 -7/11q23		#3	M4	NN	1	R		ı	1	•
M2 t(6;9)/Other		#3	M4	-7/11q23	1	1	1	•	+	•
M5 t(6;9) +		#3	M2	t(6;9)/Other	1	•	1	ī	1	1
M1 NN M2 NN - + + M2 +21 + + +		#3	M_{5}	t(6;9)	+	ı	ı		ı	,
M2 NN - + M2 +21 + +		#3	M1	NN		•	•		•	
M2 +21 - +		#3	M2	N	ī	+	•	1	1	
		#3	M2	+21	ı	+	t	,	ı	

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase Table 9: Characteristics of cluster #4 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$ mutation in CEBPA, ND: not determined). S

CEBPA	1	+	1	•	•	+	1	•	+	+	+	ı	+	+	+
EVII		1	ı	1	1		1	•	·	•	1	ı			•
N-RAS K-RAS	•	1	1	•	1		•	•	•	,	t	ı		•	
N- RAS		•	1	,	ı	ı	1	•	•	ı	•	•	+	•	•
FLT3 TKD	•	1	•	•	1	1	,	,	ı	,	•	•	1	ı	•
FLT3 ITD		ı	,	ı	1	1	1	,	t	+	1	ı	ı	ı	•
Karyotype	NN	-9d	Complex	NN	Complex (+8, +11)	NN	0ther	NN	NN/11q23 (sMLL)	NN	NN	NN	NN	-9 q	NN
FAB	M1	M1	\mathbf{M}_0	M1	N	M1	M1	M1	M1	M1	M1	M1	M1	M1	M1
Cluster	#4	#4	#4	#4	#4	#4	#4	#4	#4	#4	#4	#4	#4	#4	#4
Patient	3327	2242	2668	2238	3314	2686	3483	3491	2218	1316	2273	2545	2169	2753	2192
		10					15					20			

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 10: Characteristics of cluster #5 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$ mutation in CEBPA, ND: not determined). C

	Patient	Cluster	FAB	Karyotype	$FLT3~{ m ITD}$	$FLT3\mathrm{TKD}$	N-RAS	K- RAS	EVII	CEBPA
	3301	#2	M_{2}	-5/7(q)	1	+	+		+	t
10	2228	#2	M4	NN	ı	ı	+	1	+	t
	2272	42	M5	+8/Other	+	1		1	ı	ı
	2525	42	M5	NN	1	·	R	ND	•	,
	2655	42	M4	ND	•			+	1	ı
	2278	#2	M5	NN	,		,	1	1	1
15	2283	42	M4	+8/Other	•	ì	ı	1	•	,
	2279	42	M4	NN	•	•	1	•		•
	2259	£	M4	Complex	r	•		•	•	
	2220	42	M5	+11	•		,	•		•
	3490	42	M5	0ther	1		ī	1	•	•
20	2217	#2	M5	+8/Other	•	+				+
	3486	42	M4	NN	•	•	•	1		ı
	3097	42	M4	+8/0ther			•	ı		,
	2687	ŧ	M5	NN	•	1	•	•	•	1
	3325	第	M4	NN	•	1	r	•	,	ı
25	2467	42	M5	N QN	•	1	•	t		
	2244	3	M5	+8/3q/Other	ı	ı	,	+	•	1
	2282	#2	M4	NN	1	ı	ı	ı		ı
	2771	42	M5	NN	ī	+	•		1	1

	Table 10	Table 10 (continued):	.:							
	Patient	Cluster	FAB	Karyotype	FLT3 ITD	FLT3 TKD	N- RAS	K- RAS	EVII	CEBPA
	2185	42	M_{2}	NN	+	ı	1	,	•	
က	3484	42	M4	NN	1	1	1	•		ı
	2191	\$	R	NN	1	1	•	+		
	3321	.2#	M5	8+	+	ı	1	•	,	•
	3493	#2	M5	Other	,	1		•		
	2296	4	M5	NN	+	1	•			:
10	2231	42	M4	NN	+	,				1
	2227	£	M_{2}	NN/11q23 (sMLL)	ı	+		1		•
	2275	42	M5	NN	+	1	ı		•	ı
	2692	42	M5	NN	+	t	1	ì		ì
	2174	42	M5	NN	ı	1	+			ı
15	5669	42	M_{2}	NN	+	ı	t	1	1	
	2175	42	M5	NN	t	ı	•	ì		1
	2291	42	M5	+8	1	+	ĭ	1	τ	1
	2670	42	M5	t(6;9)	+	•	ı	1		1
	2289	9#	M5	NN	+	+	•	1	ı	1
20	2181	#2	M5	NN	+	•		,	,	ı
	2198	42	M5	NN	ı	ı	•	1		t
	3482	42	M5	NN	+	ı	1	•		
	1482	42	M4	NN		ı	+	+	•	•
	2176	£	M4	NN	+		•	•	1	ı
25	2305	9#	M5	NN	+	1	ı	t	1	•
	2534	9#	M2	Complex	,	•	•	1	ı	1
	1197	#2	M0	Complex	•		1	t		•

domain mutation in FLT3; N. or K-RAS: mutation in codon 12,13 or 61 of N. or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 11: Characteristics of cluster #6 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$ mutation in CEBPA, ND: not determined). 10

CEBPA								
EVII		,			•			1
K- RAS	1	+	+	•	1	•	•	
N-RAS								
$FLT3\mathrm{TKD}$	ı	1				ı		+
FLT3 ITD	+	+	+	+	+	+	+	+
Karyotype	NN	R						
FAB	M2	M1	M2	M1	M1	M2	M1	M1
Cluster	9#	9#	9#	9#	9#	9#	9#	9#
Patient	2683	1063	3333	2248	2203	2679	2644	2173

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 12: Characteristics of cluster #7 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 mutation in CEBPA, ND: not determined). 20

70000	CEBFA	1	ı	ı	ı	•	1	1	t	1	•	1	•	•	ì	•	1	•	•
17777	EV11	1	1	t	•		•	•		•	•	1		1	•	•	+	1	+
74 tr 74	K-KAS	ı	1	1	•	1	•	1	•	,	•	ı	ı	ı	ı	,		8	,
57.6	N-KAS	1	t		·		•	•	•		ı	ı	•				ı		1
CELEBORAL SERVICES	FLTSTKD	1	1	ſ	ì	t	•	,	ı	t	•	ī	·	ı	•	ı	ı	•	•
CHILL OF THE	FLTSIID	•	1	+	ı	+	+	,	ı	t	•	+		•	t	ı	ı	t	•
	Karyotype	NN	NN	NN	NN	NN	NN	Other	NN	NN	Other	NN	NN	Other	+8/0ther	Complex(3q/+8)	NN	NN	ON
ļ	FAB	m M2	M3	M1	M1	M1	M2	M2	M6	M1	M6	M6	M_{2}	R	M2	M2	M1	M2	M3
	Cluster	L #	L #	L #	L #	<i>L#</i>	<i>L#</i>	L #	L #	<i>L</i> #	L #	L #	<i>L</i> #	L #	L #	<i>L#</i>	<i>L#</i>	L #	<i>L#</i>
	Patient	3310	3098	2199	2769	2268	2507	3489	2284	2246	2224	2490	3319	3334	2544	2251	2222	2252	3293
			10					15					20					25	

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 13: Characteristics of cluster #8 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 mutation in CEBPA, ND: not determined). ည

CEBPA	1	•	,		,	1	1	1	•	1	1	1	1	,
EVII	1	ı	1		ı	•			ı	1		•	Î	1
N-RAS K-RAS	t	t	t		t		r		•	ı			1	ı
N-RAS	ı		1		ı	1	+	1		ı	1	ı	1	•
$FLT3~\mathrm{TKD}$	ı	ı	1		•	t	t	1	1	t	t	•	•	1
FLT3 ITD	,	1	ı	d)	ı	t	,		ı		•	•	,	1
Karyotype	+21	Complex $(-7(q)/+8)$	Complex	(11q23 (t(8;11)), -5, 3q)	+11/0ther	NN	+8,-7(q)	NN	inv7(q)/other	£-,	NN	0ther	Other	NN
FAB	M2	M5	M2		QN	M2	R	M2	M2	M2	M2	M2	M0	M2
Cluster	8#	8#	8#		8#	#8	8#	8#	8#	8#	#8	#8	8#	8#
Patient	2223	2514	3318		3481	3485	3315	2256	3326	2656	2543	2290	2304	2756
		10					15					20		

abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 14: Characteristics of cluster #9 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23, 11q23,$ (NN) are indicated, BP:inv(16) breakpoint, RT: real-time PCR for CBF 8-MYH11 (Primer CBF8 5'-

FAM 5'-TGGAGTTTGATGAGGAGGGAGCCC-3' TAMRA); FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: AAGACTGGATGGTATGGGCTGT-3' (sense), Primer 126REV 5'-CAGGGCCCGCTTGGA-3' (antisense), Probe CBFB 6tyrosine kinase domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or K-RAS; EVII: EVII overexpression; CEPBA: mutation in CEBPA, ND: not determined). rO

10	Patient	Cluster	FAB	Karyotype	BP	RT	FLT3 ITD	$FLT3~\mathrm{TKD}$	N- RAS	K-RAS	EVII	CEBPA
	3277	6#	M1		A	+	ı	ı	1	1		1
	3286	6#	M4		Ą	+	ı	1	+	1	•	•
	3309	6#	M4		A	+	ı	+	+	,	•	
	3115	6#	M5		A	+		ı	ı	•		
15	2235	6#	M4		A	+	,	ŧ	1	•	•	1
	2293	6#	M4		A	+	ı	ı		•	1	1
	5696	6#	M4		A	+		ı	+	•		1
	3324	6#	M5		A	+	1	,	1		1	1
	2647	6#	M4		Ą	+	ı	+	ı	t	t	1
20	2172	6#	M4		A	+	t	+	+	•		ı
	2254	6#	M4		A	+	ı	•		,	1	ı
	2287	6#	M4		D	+	ı	+		,	,	ı
	2189	6#	M4		A	+	ı	•	+	,	1	t
	2766	6#	M4		A	+	•	+	1		ı	1
25	2249	6#	M5		Ą	+	ı	+	•		1	1
	2215	6#	M4		A	+	ī		+	1		1

Table 14: (continued)

CEBPA	•		•	1	·	•	,
EVII	•	•	ı	1	1	•	ŧ
K-RAS		t	+	•	•	,	
N-RAS							
FLT3 TKD	1	ı	1		ì		•
FLT3 ITD	1	1	ı	ı	,	ı	•
\mathbf{RT}	+	+	+	+	+	+	+
BP	A	A	A	A	A	A	A
Karyotype	idt(16)	idt(16)	idt(16)	idt(16)	NN	idt(16)/+8	idt(16)
FAB	M4	M4	N	M4	M4	M2	M4
Cluster	6#	6#	6#	6#	6#	6#	6#
Patient	2678	2202	3487	3329	2274	2750	3285
		ಬ					

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 15: Characteristics of cluster #10 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 mutation in CEBPA, ND: not determined). 70

CEBPA		•	•	ı	1	1	1	1	t	ı	ı	ı	+	•	1	1	1	1
EVII +																		
K-RAS	1 1	•	3		ı			1	ı	•	ı	1	1	ı	1	ı	1	
N-RAS		•	ı		+	ı	•	1	1	+	1	1	ı	ı	1	+	1	•
FLT3 TKD		ı		•	•	+	1	ı	1	•	1	1	•	,	1		1	ı
FLT3 ITD	. ,	+	t	,	1	1	1	1	ı	1	,	ı	1	•	•	+	1	+
Karyotype ND	-7 -7/3q	-7(q)	Other	0ther	+11	t(9;22)	8+	ن -	0ther	-7/3q	ND	-7(q)	Other	QN QN	<i>L</i> -	NN	<i>L</i> .	NN
FAB M4	M2 M5	M2	M5	Mo	M1	M1	M1	M_{2}	M0	M0	M5	M1	M1	Q.	M1	M2	M5	M1
Cluster #10	#10 #10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10	#10
Patient 2661	$3102 \\ 2747$	2327	2551	2276	2226	3308	2546	2757	3313	2664	2666	1188	2550	2539	2250	2773	2186	2301
(*	10				15					20					25			

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(continued)	
e 15:	
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Karyotype	Other	Other
	M1	
Cluster	#10	#10
Patient	2497	2247
		က

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 16: Characteristics of cluster #11 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 mutation in CEBPA, ND: not determined). က

EVII									
K-RAS	•	•	•	•	•	•	•	ı	•
N-RAS		ı	ı	ı		ı		+	+
$FLT3~\mathrm{TKD}$	1	+	+	+	•	r		1	,
$FLT3~{ m ITD}$	1	•	•	•	+	ľ	•	ı	,
Karyotype	Other	NN	Other	NN	NN	NN	NN	NN	NN
									M5
Cluster	#11	#11	#11	#11	#11	#11	#11	#11	#11
Patient	2209	3096	2239	2261	1299	1432	3311	1766	2206
		10					15		

(NN) are indicated, RT: real-time PCR for PML-RARα (Primer PML3-for 5'-CCCCAGGAGCCCCGT-3' (sense), Primer PMLabnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype kbr 5'-CCTGCAGGACCTCAGCTCTT-3'(sense), Primer RAR4-rev 5'- AAAGCAAGGCTTGTAGATGCG-3'(antisense), Probe RARA 6-FAM 5'-AGTGCCCAGCCCTCCCTCGC-3' TAMRA); FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: Table 17: Characteristics of cluster #12 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB tyrosine kinase domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or K-RAS; EVII: EVII subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 overexpression; CEPBA: mutation in CEBPA, ND: not determined).

	_																
,	EVII	•	,	,	z	ı	ı		ı	ı					ı		ì
í	K- RAS	•	•		•	•	•	,		•				•		•	ı
6	N- RAS	ı	1	,	•		•	ı		•	•				ì	1	1
	FLT3 TKD		ı	+	1		+	+		1	ı	+	•		+	•	
	$FLT3~{ m ITD}$	1	,		1	1			ı		,	1	+	+	,	+	•
	RT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	Karyotype	t(15;17)	t(15;17)/Other	t(15;17)/Other	t(15;17)	t(15;17)/Other	t(15;17)	t(15;17)	t(15;17)	t(15;17)	t(15;17)						
	FAB	M3	M3	M3	M3	M2	M3	M3	M3	M3							
	Cluster	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12	#12
	Patient	2466	2509	2219	2263	2307	2510	2297	2265	2266	3279	2170	2680	2671	2516	2468	3278
	10					15					20					25	

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CEBPA	1		1
EVI1	•	1	1
K- RAS		1	1
N- RAS			
$FLT3\mathrm{TKD}$	ı	•	ı
FLT3 ITD	+	+	+
\mathbf{RT}	+	+	+
Karyotype	$Other^*$	t(15;17)/Other	t(15;17)/+8
FAB	M3	M4	M3
Cluster	#12	#12	#12
Patient	322	2179	1448
		ರ	

^{*}Full karyotype of patient 322: 46,XX, add(12)(p1?3).

abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype (NN) are indicated, RT: real-time PCR for AML1-ETO (Primer 821 For 5'-TCACTCTGACCATCACTGTCTTCA-3' (sense), Table 18: Characteristics of cluster #13 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB $subtype\ of\ AML;\ Karyotype:\ t(15;17),\ t(8;21),\ inv(16)/t(16;16), +8, +11, +21, -5(q), -7(q), t(9;22), 3q\ abnormalities,\ 11q23$

ACCCACCGCAAGTCGCCACCT -3' TAMRA); FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase domain mutation in FLT3; N. or K-RAS: mutation in codon 12,13 or 61 of N. or K-RAS; EVII: EVII overexpression; CEPBA: mutation in CEBPA, ND: not determined).

Primer 821 Rev 5'-ATTGTGGAGTGCTTCTCAGTACGAT -3'(antisense), Probe ETO 6- FAM 5'-

10	Patient	Cluster	FAB	Karyotype	RT	FLT3 ITD	$FLT3\mathrm{TKD}$	N- RAS	K- RAS	EVII	CEBPA
	2243	#13	M2	t(+8;21)/Other	+	ı		ı		,	+
	2658	#13	M4	t(+8;21)	+	1	•	•			ı
	2752	#13	M2	t(+8;21)	+	,					1
	2197	#13	M2	t(+8;21)/Other	+	+	ι				1
15	2245	#13	M2	t(+8;21)/Other	+	1	+	•			1
	3332	#13	M2	t(+8;21)	+	,		•			,
	2262	#13	M2	t(+8;21)/Other	+	•	ı	t		ı	1
	2178	#13	M2	t(+8;21)/Other	+	•	1	,			t
	2511	#13	M2	t(+8;21)/+8/Other	+		ı			•	,
20	2200	#13	M2	t(+8;21)/Other	+	1	1	ı			i
	2208	#13	M2	t(+8;21)	+	•		•			1
	3295	#13	M2	t(+8;21)	+		•	t			•
	2204	#13	M2	t(+8;21)/Other	+	•		+		1	1
	3292	#13	M2	t(+8;21)	+		t	•		1	ı
25	2549	#13	M2	t(+8;21)/Other	+	1	1	ì			•
	2267	#13	M2	t(+8;21)/Other	+	1	ı			1	ı
	2695	#13	M1	t(+8;21)	+	1	t	1	1	ı	1

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7	×	5

CEBPA	•	1	•	r	ı
EVII	•	•	•	•	
K- RAS	+		•	•	ı
N-RAS		,	,	+	+
FLT3 TKD	•	•	ı	ı	
FLT3 ITD	•	1		ı	1
RT	+	+	+	+	+
Karyotype	t(+8;21)/Other	t(+8;21)/Other	t(+8;21)/Other	t(+8;21)/Other	t(+8;21)/Other
FAB	M2	M2	M2	M2	M2
Cluster	#13	#13	#13	#13	#13
Patient	2751	2211	2764	2210	2762
		က			

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 19: Characteristics of cluster #14 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 ည

mutation in CEBPA, ND: not determined).

CEBPA	1	ı	i	ı	1	1	ı	t
EVII		•	ı	*			1	•
N-RAS K-RAS	•		٠	•	ı			1
			+	1	ı	ı	•	ı
FLT3 TKD	ı	1	ı	,	ı	ı	+	ı
FLT3 ITD	1	+	1	+	1	1	ı	r
Karyotype	ND	ND QN	+8/Other	11q23 (ND)	-5(q)	Complex(-5/-7/+8)	Complex	8+
FAB	R	M2	M2	M2	M2	M1	M4	M2
Cluster	#14	#14	#14	#14	#14	#14	#14	#14
Patient	2536	2704	2690	3289	2212	2233	1201	2188
		10					15	

+

Z Z

M2 M5

#14 #14

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 20: Characteristics of cluster #15 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 mutation in CEBPA, ND: not determined). rO

		+						
EVII	•					1	•	
K-RAS	ı		•	ı	1	3	,	
N-RAS	,	1	1	+	•	i	1	,
FLT3 TKD	+	ľ	ı	i	ı	1	,	ı
FLT3 ITD	,		ı	+	r	+	ı	•
Karyotype	NO	NN	NN	NN	Other	NN	NN	-7/Other
		M4						
Cluster	#15	#15	#15	#15	#15	#15	#15	#15
Patient	2767	2748	2240	3101	2234	2230	2253	2237
		10					15	

domain mutation in FLT3; N- or K-RAS: mutation in codon 12,13 or 61 of N- or KRAS; EVII: EVII overexpression; CEPBA: abnormalities (translocation/self fusion (sMLL)), complex(abnormalities involved) (>3abnormalities) and normal karyotype Table 21: Characteristics of cluster #16 (Patient: patient number, Cluster: cluster number (2856 probe sets); FAB: FAB (NN) are indicated, RT: real-time PCR; FLT3 ITD: internal tandem duplication in FLT3; FLT3 TKD: tyrosine kinase subtype of AML; Karyotype: t(15;17), t(8;21), inv(16)/t(16;16),+8,+11,+21,-5(q),-7(q),t(9;22),3q abnormalities, 11q23 mutation in CEBPA, ND: not determined). rO

CEBPA	ı	,	ı	1	1	1		1	ı	ı	•
EVII				•	1	•	1	ı	•	•	1
N-RAS K-RAS	ı	•	•	1	•	ı	•			1	
			•	•	•	•	t		•	1	
FLT3 TKD	•	•	,	•	+	•	ı		1	•	1
FLT3 ITD	•	1	·	1	1	1	1	,	ı	1	1
Karyotype	NN	Other	0ther	+8/11q23 (t(11;19)	11q23 (t(9;11))	Other/11q23 (t(9;11))	11q23 (t(9;11))	Other	NN	NN	11q23 (t(9;11))/-7
FAB	M4	M5	M5	M5	m M5	M5	M5	M5	M5	M1	M5
Cluster	#16	#16	#16	#16	#16	#16	#16	#16	#16	#16	#16
Patient	2225	2184	2535	3322	2285	3316	2694	3317	2749	2281	2541
		10					15				

Table 22: Frequency and percentage of cytogenetic and molecular abnormalities of all AML patients within each of the assigned clusters. All patients with a specific abnormality were considered, irrespective of the presence of additional abnormalities (NC: patients not assigned to any of the 16 clusters).

ಸರ	Cluster Patients in cluster	#1 14	#2 17	#3 19	#4 15	#5 44	9# 8	#7 18	#8 13	#9 23	#10 22	#11	#12 19	#13 22	#14 10	#15 8	#16 11	NC 13	total 285
10	Cytogenetics t(15;17)												18 (95)						18 (6)
15	t(8;21) inv(16)/t(16;16) +8 +11 +21	2 (14)	2 (12)	1 (5)	1(7)	7 (16) 1 (2)		2 (11)	2 (15) 1 (8) 1 (8)	19 (83) 2 (9)	1 (5) 1 (5)		1 (5)	22 (100) 1 (5) 3	3 (30)		1 (9)	2 (15) 1 (8)	22 (8) 19 (7) 19 (7) 7 (2) 2 (1)
	-5 -5(q) -7 -7(q)			1 (5)		1 (2)			1 (8) 1 (8) 3 (23)	2 (9)	1 (5) 5 (23) 2 (9)				1 (10) 1 (10) 1 (10)	1 (13)	1 (9)	2 (15)	3 (1) 1 (<1) 13 (5) 7 (2)
20	3q t(6;9) t(9;22) +(1,1,29)	(4.8)	1 (6)	2 (11) 1 (5)	9 (13)	1 (2)		1 (6)	1 (8)		1 (5)				1 (10)		5 (45)	1 (8)	4 (1) 4 (1) 2 (1) 19 (7)
25	complex (>3 abn.) other non-complex normal ND	1 (7) 2 (14) 6 (43)	1 (6) 13 (76)	2 (11) 3) 13 (68)	2 (13) 2 (13) 3 (20) 3 10 (67)	3 (7) 7 (16)) 27 (61) 2 (5)) 7 (88) 1 (13)	1 (6) 4 (22) 12 (67) 1 (6)	2 (15) 4 (31) 4 (31)	3 (13)	6 (27) 2 (9) 3 (14)	2 (22) 7 (78)	4 (21)	4 (21) 15 (68)	2 (20) 2 (20) 2 (20) 2 (20)	2 (25) 5 (63) 1 (13)	4 (36) 3 (27)	3 (23) 5 (38)	11 (4) 60 (21) 119 (42) 10 (4)
30	Cluster Patients in cluster	#1	#2	#3	#4	#5	9#	#7	#8	#9 23	#10	#11	#12 19	#13	#14	#15 8	#16	NC 13	total 285
	Molecular markers																		
35	FLT3-ITD FLT3-TKD N-RAS	2 (14) 14 (14 (82) 10 (53) 1 3 (18) 3 (16)	5	6 (14) 1 6 (14) 1 4 (9)	1 (13)	1 (13)	1 (8)	6 (26). 8 (35)	4 (18) 1 (5) 3 (14)	1 (11) 3 (33) 2 (22)	6 (32) 5 (26)	1 (5) 1 (5) 3 (14)	3 (30) 2 (20) 1 (10)	2 (25) 1 (13) 1 (13)	1 (9)	8 (62) 2 (15)	78 (27) 33 (12) 26 (9) 9 (3)
40	K-KAS EVII CEBPA	1 (7) 5 (36)	1 (6)	2 (11)	8 (5	2 (5) 1 (2) 2 (3)	(cz) z	2 (11)		T (#)	10 (45) 1 (5)			1 (5)		5 (63)		2 (15)	

Table 23: Top40 genes of cluster #1

	Probe Set	\mathbf{Gene}	Locus Link	Accession	Score	q-value SAM
	\mathbf{ID}	symbol	${f number}$	number	SAM	(%)
	$220014_{ m at}$	LOC51334	51334	NM_016644.1	7,09	1,96
5	206762 _at	KCNA5	3741	NM_002234.1	6,68	1,96
	$213094_{ t at}$	GPR126	57211	AL033377	6,18	1,96
	218502_s_at	TRPS1	7227	NM_014112.1	5,95	1,96
	221530_s_at	BHLHB3	79365	AB044088.1	5,63	1,96
	$221884_{ extbf{at}}$	EVI1	2122	BE466525	5,40	1,96
10	203642_s_at	KIAA0977	22837	NM_014900.1	4,96	1,96
	$212827_{ m at}$	IGHM	3507	X17115.1	4,85	1,96
	205612_at	MMRN	22915	NM_007351.1	4,72	1,96
	209200_at	MEF2C	4208	N22468	4,59	1,96
	214255_at	ATP10A	57194	AB011138.1	4,41	1,96
15	201539_s_at	FHL1	2273	U29538.1	4,37	1,96
	205717_x_at	PCDHGC3	5098	NM_002588.1	4,29	1,96
	222144_at	KIF17	57576	AA909345	4,25	1,96
	219922_s_at	LTBP3	4054	NM_021070.1	4,21	1,96
	215836_s_at	PCDHGC3	5098	AK026188.1	4,20	1,96
20	205861_at	SPIB	6689	NM_003121.1	4,15	1,96
	203372_s_at	SOCS2	8835	AB004903.1	4,12	1,96
	209079_x_at	PCDHGC3	5098	AF152318.1	4,11	1,96
	215811_at		~	AF238870.1	4,09	1,96
	209199_s_at	MEF2C	4208	N22468	4,08	1,96
25	207655_s_at	BLNK	29760	NM_013314.1	4,05	1,96
	203716_s_at	DPP4	1803	M80536.1	4,03	1,96
	219737_s_at			AI524125	4,01	1,96
	204304_s_at	PROM1	8842	NM_006017.1	3,97	1,96
	203373_at	SOCS2	8835	NM_003877.1	3,95	1,96
30	218237_s_at	SLC38A1	81539	NM_030674.1	3,87	1,96
	202265at	BMI1	648	NM_005180.1	3,86	1,96
	210298_x_at	FHL1	2273	AF098518.1	3,83	1,96
	208436_s_at	IRF7	3665	NM_004030.1	3,77	1,96
	210032_s_at	SPAG6	9576	AI651156	3,77	1,96
35	222088_s_at	SLC2A14	144195	AA778684	-3,76	1,96
	204621_s_at	NR4A2	4929	AI935096	-3,80	1,96
	216248_s_at	NR4A2	4929	S77154.1	-3,84	1,96
	216236_s_at	SLC2A14	144195	AL110298.1	-3,85	1,96
	204622_x_at	NR4A2	4929	NM_006186.1	-3,85	1,96
40	202497_x_at	SLC2A3	6515	NM_006931.1	-3,91	1,96
	201464_x_at	JUN	3725	$\overline{\mathrm{BG491844}}$	-3,92	1,96
	202672_s_at	ATF3	467	NM_001674.1	-4,11	1,96

Table 24: Top40 genes of cluster #2

	Probe Set	Gene	Locus Link	Accession	Score	q-value SAM
	\mathbf{ID}	symbol	number	number	SAM	(%)
	207034_s_at	GLI2	2736	NM_030379.1	10,30	1,04
5	206341_at	IL2RA	3559	NM_000417.1	9,15	1,04
	211269_s_at	IL2RA	3559	K03122.1	8,24	1,04
	215288_at	TRPC2	7221	AI769824	7,44	1,04
	205190_at	PLS1	5357	$NM_002670.1$	7,34	1,04
	210145_at	PLA2G4A	5321	M68874.1	7,31	1,04
10	204341_at	TRIM16	10626	$NM_006470.1$	7,23	1,04
	206574_s_at	PTP4A3	11156	$NM_007079.1$	7,01	1,04
	203187_at	DOCK1	1793	NM_001380.1	6,48	1,04
	219615_s_at	KCNK5	8645	$NM_003740.1$	6,29	1,04
	212276_at	LPIN1	23175	D80010.1	6,05	1,04
15	206298_at	RhoGAP2	58504	$NM_021226.1$	5,82	1,04
	207533_at	CCL1	6346	NM_002981.1	5,69	1,04
	206582_s_at	GPR56	9289	NM_005682.1	5,41	1,04
	208797_s_at	GOLGIN-6'	7 23015	AI829170	5,37	1,04
	205453_at	HOXB2	3212	NM_002145.1	5,12	1,04
20	212070_at	GPR56	9289	$\overline{\mathrm{AL554008}}$	5,01	1,04
	209409_at	GRB10	2887	D86962.1	4,99	1,04
	210425_x_at	GOLGIN-6		AF164622.1	4,97	1,04
	208767_s_at	LAPTM4B	55353	AW149681	4,95	1,04
	221942_s_at	GUCY1A3	2982	AI719730	4,95	1,04
25	209193_at	PIM1	5292	M24779.1	4,94	1,04
	204030_s_at	SCHIP1	29970	NM_014575.1	4,89	1,04
	213844_at	HOXA5	3202	NM_019102.1	4,74	1,04
	208798_x_at	GOLGIN-6		AF204231.1	4,70	1,04
	216268_s_at	JAG1	182	U77914.1	4,68	1,04
30	208792_s_at	CLU	1191	M25915.1	4,60	1,04
00	217414_x_at			V00489	-4,62	1,04
	211699_x_at	HBA1	3039	AF349571.1	-4,67	1,04
	217232_x_at			AF059180	-4,71	1,04
	209116_x_at	$_{ m HBB}$	3043	M25079.1	-4,71	1,04
35	214414_x_at	HBA1	3039	T50399	-4,72	1,04
00	211696_x_at	HBB	3043	AF349114.1	-4,72	1,04
	211745_x_at	HBA1	3039	BC005931.1	-4,75	1,04
	204018_x_at	HBA1	3039	NM_000558.2	-4,83	1,04
	208623_s_at	VIL2	7430	J05021.1	-4,91	1,04
40	209458_x_at	HBA1	3039	AF105974.1	-4,96	1,04
-0	214582_at	PDE3B	5140	NM_000753.1	-5,29	1,04
	213152_s_at			AI343248	-5,39	1,04
	206571_s_at	MAP4K4	9448	NM_004834.1	-6,87	1,04
				·-·-		•

Table 25: Top40 genes of cluster #3

Probe Set Gene Locus Link Accession Score	
ID symbol number number SAM	(%)
206950_at SCN9A 6335 NM_002977.1 10,09	0,21
5 205848_at GAS2 2620 NM_005256.1 8,63	0,21
207533_at CCL1 6346 NM_002981.1 8,56	0,21
205190_at PLS1 5357 NM_002670.1 7,94	0,21
213110_s_at COL4A5 1287 AW052179 7,51	0,21
208767_s_at LAPTM4B 55353 AW149681 7,09	0,21
10 206298_at RhoGAP2 58504 NM_021226.1 7,07	0,21
208029_s_at LAPTM4B 55353 NM_018407.1 7,05	0,21
204044_at QPRT 23475 NM_014298.2 7,04	0,21
202889_x_at ANPEP 9053 T62571 6,84	0,21
217975_at LOC51186 51186 NM_016303.1 6,81	0,21
15 201664_at SMC4L1 10051 AL136877.1 6,81	0,21
210116_at SH2D1A 4068 AF072930.1 6,74	0,21
213217_at ADCY2 108 AU149572 6,53	0,21
204160_s_at ENPP4 22875 AW194947 6,48	0,21
204341_at TRIM16 10626 NM_006470.1 6,42	0,21
20 214039_s_at LAPTM4B 55353 T15777 6,41	0,21
206582_s_at GPR56 9289 NM_005682.1 6,28	0,21
202890_at MAP7 9053 T62571 6,28	0,21
215471_s_at MAP7 9053 AJ242502.1 6,23	0,21
219602_s_at FLJ23403 63895 NM_022068.1 6,20	0,21
25 219304_s_at SCDGF-B 80310 NM_025208.1 6,05	0,21
203187_at DOCK1 1793 NM_001380.1 6,03	0,21
215388_s_at HFL1 3078 X56210.1 6,00	0,21
201663_s_at SMC4L1 10051 NM_005496.1 6,00	0,21
214228_x_at TNFRSF4 7293 AJ277151 5,96	0,21
30 201427_s_at SEPP1 6414 NM_005410.1 5,94	0,21
207838_x_at PBXIP1 57326 NM_020524.1 5,92	0,21
201829_at NET1 10276 AW263232 5,85	0,21
220377_at C14orf110 29064 NM_014151.1 5,85	0,21
203973_s_at KIAA0146 23514 NM_005195.1 -5,88	0,21
35 205707_at IL17R 23765 NM_014339.1 -5,95	0,21
212195_at IL6ST 3572 AL049265.1 -6,03	0,21
206034_at SERPINB8 5271 NM_002640.1 -6,11	0,21
203773_x_at BLVRA 644 NM_000712.1 -6,71	0,21
221830_at RAP2A 5911 AI302106 -6,94	0,21
40 218831_s_at FCGRT 2217 NM_004107.1 -7,10	0,21
211729_x_at BLVRA 644 BC005902.1 -7,18	0,21
204500_s_at AGTPBP1 23287 NM_015239.1 -8,15	0,21
212543_at AIM1 202 U83115.1 -8,19	0,21

Table 26: Top40 genes of cluster #4

	Probe Set	Gene	Locus Link	Accession	Score	q-value SAM
	ID	symbol	number	number	SAM	(%)
_	216286_at			AV760769	13,34	0,11
5	216191_s_at	TRD@	6964	X72501.1	13,01	0,11
	206232_s_at	B4GALT6	9331	NM_004775.1	12,59	0,11
	213830_at	TRD@	6964	AW007751	11,85	0,11
	211682_x_at	UGT2B28	54490	AF177272.1	11,60	0,11
	219383_at	FLJ14213	79899	NM_024841.1	11,57	0,11
10	217143_s_at	TRD @	6964	X06557.1	11,55	0,11
	214551_s_at	CD7	924	$NM_006137.2$	11,22	0,11
	214049_x_at	CD7	924	AI829961	11,04	0,11
	213 9 10_at	IGFBP7	3490	AW770896	10,85	0,11
	207996_s_at	C18orf1	753	$NM_004338.1$	10,65	0,11
15	220567_at	ZNFN1A2	22807	NM_016260.1	10,27	0,11
	209994_s_at	ABCB1	5243	AF016535.1	9,90	0,11
	206233_at	B4GALT6	9331	AF097159.1	9,66	0,11
	217147_s_at	TRIM	$\boldsymbol{50852}$	AJ240085.1	9,44	0,11
	209993_at	ABCB1	5243	AF016535.1	9,40	0,11
20	210448_s_at	P2RX5	5026	U49396.1	9,36	0,11
	216525_x_at	PMS2L9	5387	D38437.1	9,20	0,11
	54037_at	HPS4	89781	AL041451	9,16	0,11
	206726_at	PGDS	27306	NM_014485.1	8,79	0,11
	202242_at	TM4SF2	7102	$NM_004615.1$	8,79	0,11
25	203987_at	FZD6	8323	NM_003506.1	8,63	0,11
	214757_at			BG178274	8,50	0,11
	205884_at	ITGA4	3676	NM_000885.2	8,49	0,11
	213416_at	ITGA4	3676	BG532690	8,37	0,11
	218627_at	FLJ11259	55332	NM_018370.1	-8,51	0,11
30	208923_at	CYFIP1	23191	BC005097.1	-8,75	0,11
00	219371_s_at	KLF2	10365	NM_016270.1	-8,95	0,11
	203233_at	IL4R	3566	NM_000418.1	-8,96	0,11
	205382_s_at	DF	1675	NM_001928.1	-8,98	0,11
	208683_at	CAPN2	824	M23254.1	-9,08	0,11
35	201160_s_at	CSDA	8531	AL556190	-9,13	0,11
00	201412_at	LRP10	26020	NM_014045.1	-9,19	0,11
	202252_at	RAB13	5872	NM_002870.1	-9,25	0,11
	217800_s_at	NDFIP1	80762	NM_030571.1	-9,98	0,11
	202241_at	C8FW	$\boldsymbol{10221}$	NM_025195.1	-10,41	0,11
40	209191_at	TUBB-5	84617	BC002654.1	-10,60	0,11
_0	200765_x_at	CTNNA1	1495	NM_001903.1	-14,35	0,11
	200764_s_at	CTNNA1	1495	AI826881	-15,70	0,11
	210844_x_at	CTNNA1	1495	D14705.1	-15,91	0,11
	410044_X_at	OTMINET	1430	17 T# 100.T	-10,01	·,

Table 27: Top40 genes of cluster #5

Table 21: Top	40 genes of ciu	ster #0			
Probe Set ID			Accession number	Score SAM	q-value SAM (%)
206710 s at	EPB41L3	23136	NM_012307 ₋ 1	21,03	0,05
	LILRB1	10859	NM_006863.1	19,91	0,05
	EPB41L3	23136	BC006141.1	19,65	0,05
206934_at	SIRPB1	10326	NM_006065.1	19,55	0,05
219788_at	PILRA	29992	NM_013439.1	17,93	0,05
204392_at	CAMK1	8536	$NM_003656.2$	17,41	0,05
219872_at	DKFZp434L142	51313	NM_016613.1	17,11	0,05
212681_at	EPB41L3	23136	AI770004	17,04	0,05
214590_s_at	${ m UBE2D1}$	7321	AL545760		0,05
204254_s_at	VDR	7421	$NM_000376.1$	•	0,05
203767_s_at	STS	412	AU138166		0,05
207224_s_at	SIGLEC7		$NM_016543.1$		0,05
206278_at	PTAFR		D10202.1		0,05
204619_s_at	CSPG2	1462	BF590263		0,05
219593_at	PHT2	51296	$NM_016582.1$		0,05
220832_at	TLR8	51311	$NM_016610.1$		0,05
210146_x_at	LILRB3	11025	AF004231.1		0,05
222218_s_at		29992	AJ400843.1		0,05
203768_s_at		412			0,05
204858_s_at		1890			0,05
		10859			0,05
					0,05
					0,05
	•				0,05
-				•	0,05
_					0,05
					0,05
					0,05
			-	•	0,05
					0,05
				•	0,05
					0,05
			_	•	0,05
					0,05
					0,05
					0,05
					0,05
				-	0,05
					0,05
50221_at	TFEB	7942	A1524138	13,81	0,05
	Probe Set ID 206710_s_at 207872_s_at 207872_s_at 211776_s_at 216934_at 219788_at 204392_at 219872_at 212681_at 214590_s_at 204254_s_at 204254_s_at 207224_s_at 204619_s_at 204619_s_at 219593_at 220832_at 210146_x_at 222218_s_at 203768_s_at	Probe Set	ID symbol number 206710_s_at EPB41L3 23136 207872_s_at LILRB1 10859 211776_s_at EPB41L3 23136 206934_at SIRPB1 10326 219788_at PILRA 29992 204392_at CAMK1 8536 219872_at DKFZp434L142 51313 212681_at EPB41L3 23136 214590_s_at UBE2D1 7321 204254_s_at VDR 7421 203767_s_at STS 412 207224_s_at SIGLEC7 27036 206278_at PTAFR 5724 204619_s_at CSPG2 1462 219593_at PHT2 51296 220832_at TLR8 51311 210146_x_at LILRB3 11025 222218_s_at PILRA 29992 203768_s_at STS 412 204858_s_at ECGF1 1890 211732_x_at HNMT 3176	Probe Set Gene Locus Link number Accession number 206710_s_at EPB41L3 23136 NM_012307.1 207872_s_at LILRB1 10859 NM_006863.1 211776_s_at EPB41L3 23136 BC006141.1 206934_at SIRPB1 10326 NM_006065.1 219788_at PILRA 29992 NM_013439.1 204392_at CAMK1 8536 NM_003656.2 219872_at DKFZp434L142 51313 NM_016613.1 212681_at EPB41L3 23136 AI770004 214590_s_at UBE2D1 7321 AL545760 204254_s_at VDR 7421 NM_000376.1 203767_s_at STS 412 AU138166 207224_s_at SIGLEC7 27036 NM_016543.1 206278_at PTAFR 5724 D10202.1 204619_s_at CSPG2 1462 BF590263 219593_at PHT2 51296 NM_016582.1 220832_at TLR8 51311	Probe Set Gene symbol symbol number number number Accession number number number SAM 206710_s_at EPB41L3 23136 NM_012307.1 21,03 207872_s_at LILRB1 10859 NM_006863.1 19,91 211776_s_at EPB41L3 23136 BC006141.1 19,65 206934_at SIRPB1 10326 NM_006065.1 19,55 219788_at PILRA 29992 NM_013439.1 17,93 204392_at CAMK1 8536 NM_003656.2 17,41 219872_at DKFZp434L142 51313 NM_016613.1 17,11 212681_at EPB41L3 23136 AI770004 17,04 214590_s_at UBE2D1 7321 AL545760 15,87 204254_s_at VDR 7421 NM_000376.1 15,69 203767_s_at STS 412 AU138166 15,64 207224_s_at PTAFR 5724 D10202.1 15,55 204619_s_at CSPG2 1462 BF590263 15,07 <

Table 28: Top40 genes of cluster #6

	Probe Set		Locus Link	Accession	\mathbf{Score}	q-value SAM
	\mathbf{ID}	symbol	number	number	SAM	(%)
	221880_s_at			AI279819	12,39	0,85
5	51158_at			AI801973	10,99	0,85
	219511_s_at	SNCAIP	9627	$NM_005460.1$	8,81	0,85
	209702_at	FTO	79068	U79260.1	8,51	0,85
	221959_at	MGC39325	90362	AK026141.1	8,40	0,85
	204984_at	GPC4	2239	NM_001448.1	8,34	0,85
10	204983_s_at	GPC4	2239	AF064826.1	8,25	0,85
	212019_at	DKFZP564M18	32 26156	AK025446.1	7,56	0,85
	215807_s_at	PLXNB1	5364	AV693216	7,42	0,85
	219602_s_at	FLJ23403	63895	NM_022068.1	6,93	0,85
	218710_at	FLJ20272	55622	NM_017735.1	6,80	0,85
15	213217_at	ADCY2	108	AU149572	6,78	0,85
	219651_at	FLJ10713	55211	NM_018189.1	6,78	0,85
	202728_s_at	LTBP1	4052	AI986120	6,64	0,85
	206377_at	FOXF2	2295	$NM_001452.1$	6,60	0,85
	219932_at	VLCS-H1	28965	NM_014031.1	6,31	0,85
20	213260_at	FOXC1	2296	AU145890	6,23	0,85
	215623_x_at	$\mathrm{SMC4L1}$	10051	AK002200.1	6,19	0,85
	201431_s_at	DPYSL3	1809	NM_001387.1	6,18	0,85
	208414_s_at	HOXB4	3214	NM_002146.1	6,17	0,85
	218786_at			NM_016575.1	6,16	0,85
25	204750_s_at	DSC2	1824	BF196457	6,16	0,85
	219036_at	BITE	80321	NM_024491.1	6,13	0,85
	215388_s_at	$\mathrm{HFL1}$	3078	X56210.1	6,12	0,85
	220898_at			$NM_024972.1$	6,08	0,85
	215573_at	CAT	847	AU147084	6,04	0,85
30	204751_x_at	DSC2	1824	NM_004949.1	6,01	0,85
	202729_s_at	LTBP1	4052	$NM_000627.1$	5,97	0,85
	213266_at	m m m	***	BF592982	5,61	0,85
	201641_at	BST2	684	$NM_004335.2$	-5,55	0,85
	215193_x_at	HLA-DRB1	3123	AJ297586.1	-5,56	0,85
35	209619_at	CD74	972	K01144.1	-5,58	0,85
	208982_at	PECAM1	5175	AW574504	-5,62	0,85
	210982_s_at	HLA-DRA	3122	M60333.1	-5,68	0,85
	211990_at	HLA-DPA1	3113	M27487.1	-5,84	0,85
	217118_s_at	KIAA0930	23313	AK025608.1	-5,87	0,85
40	205672_at	XPA	7507	NM_000380.1	-6,10	0,85
	217845_x_at	HIG1	25994	$NM_014056.1$	-6,41	0,85
	204319_s_at	RGS10	6001	NM_002925.2	-6,69	0,85
	209083_at	CORO1A	11151	U34690.1	-6,97	0,85

Table 29: Top40 genes of cluster #7

	Probe Set		Locus Link	Accession	Score	q-value SAM
	\mathbf{ID}		number	number	SAM	(%)
	206116_s_at	TPM1	7168	NM_000366.1	15,29	0,11
5	207854_at	GYPE	2996	$NM_002102.1$	13,28	0,11
	221577_x_at	PLAB	9518	AF003934.1	12,76	0,11
	56748_at	TRIM10	10107	X90539	$12,\!56$	0,11
	205390_s_at	ANK1	286	NM_000037.2	11,78	0,11
	204720_s_at	DNAJC6	9829	AV729634	11,68	0,11
10	206146_s_at	RHAG	6005	AF178841.1	11,40	0,11
	216054_x_at	MYL4	4635	X58851	11,18	0,11
	210088_x_at	MYL4	4635	M36172.1	11,16	0,11
	205391_x_at	ANK1	286	M28880.1	11,09	0,11
	207043_s_at	SLC6A9	6536	NM_006934.1	11,08	0,11
15	218864_at	TNS	7145	AF116610.1	10,98	0,11
	203911_at	RAP1GA1	5909	NM_002885.1	10,94	0,11
	214530_x_at	EPB41	2035	AF156225.1	10,93	0,11
	206647_at	$_{ m HBZ}$	3050	NM_005332.2	10,90	0,11
	211254_x_at	RHAG	6005	AF031549.1	10,88	0,11
20	207087_x_at	ANK1	286	NM_020478.1	10,84	0,11
	208352_x_at	ANK1	286	NM_020479.1	10,83	0,11
	219630_at	MAP17	10158	NM_005764.1	10,71	0,11
	208416_s_at	SPTB	6710	NM_000347.2	10,70	0,11
	208353_x_at	ANK1	286	NM_020480.1	10,70	0,11
25	205262_at	KCNH2	3757	NM_000238.1	10,67	0,11
	210395_x_at	MYL4	4635	AF116676.1	10,65	0,11
	210586_x_at	RHD	6007	AF312679.1	10,64	0,11
	210854_x_at	SLC6A8	6535	U17986.1	10,61	0,11
	220751_s_at	C5orf4	10826	NM_016348.1	10,60	0,11
30	216063_at			N55205	10,60	0,11
	217274_x_at			X52005.1	10,53	0,11
	206145_at	RHAG	6005	$NM_000324.1$	10,51	0,11
	213843_x_at	SLC6A8	6535	AW276522	10,48	0,11
	206077_at	KEL	3792	$NM_000420.1$	10,47	0,11
35	216925_s_at	$\mathrm{TAL}1$	6886	X51990.1	10,42	0,11
	221237_s_at	OSBP2	23762	NM_030758.1	10,37	0,11
	212804_s_at	DKFZP434C21	.2 26130	AK023841.1	10,27	0,11
	207793_s_at	EPB41	2035	NM_004437.1	10,24	0,11
	205389_s_at	ANK1	286	AI659683	10,21	0,11
40	201249_at	SLC2A1	6513	$NM_006516.1$	10,20	0,11
	214433_s_at	SELENBP1	8991	NM_003944.1	10,18	0,11
	218978_s_at	MSCP	51312	NM_018586.1	10,13	0,11
	201733_at	CLCN3	1182	NM_001829.1	10,12	0,11

Table 30: Top40 genes of cluster #8

ID symbol number number SAM (%)	Æ
5 201131_s_at CDH1 999 NM_004360.1 12,12 0,17 209735_at ABCG2 9429 AF098951.2 11,01 0,17 202073_at OPTN 10133 AV757675 10,88 0,17 40093_at LU 4059 X83425 10,45 0,17 212151_at PBX1 5087 BF967998 10,14 0,17 10 201333_s_at ARHGEF12 23365 NM_015313.1 9,95 0,17 210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_030607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
209735_at ABCG2 9429 AF098951.2 11,01 0,17 202073_at OPTN 10133 AV757675 10,88 0,17 40093_at LU 4059 X83425 10,45 0,17 212151_at PBX1 5087 BF967998 10,14 0,17 10 201333_s_at ARHGEF12 23365 NM_015313.1 9,95 0,17 210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_03607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
202073_at OPTN 10133 AV757675 10,88 0,17 40093_at LU 4059 X83425 10,45 0,17 212151_at PBX1 5087 BF967998 10,14 0,17 10 201333_s_at ARHGEF12 23365 NM_015313.1 9,95 0,17 210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
40093_at LU 4059 X83425 10,45 0,17 212151_at PBX1 5087 BF967998 10,14 0,17 10 201333_s_at ARHGEF12 23365 NM_015313.1 9,95 0,17 210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C50rf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
212151_at PBX1 5087 BF967998 10,14 0,17 10 201333_s_at ARHGEF12 23365 NM_015313.1 9,95 0,17 210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
10 201333_s_at ARHGEF12 23365 NM_015313.1 9,95 0,17 210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
210430_x_at RHD 6007 L08429.1 9,72 0,17 205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
205391_x_at ANK1 286 M28880.1 9,53 0,17 221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
221237_s_at OSBP2 23762 NM_030758.1 9,53 0,17 214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
214464_at CDC42BPA 8476 NM_003607.1 9,44 0,17 15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
15 220751_s_at C5orf4 10826 NM_016348.1 9,42 0,17 202364_at MXI1 4601 NM_005962.1 9,29 0,17	
202364_at MXI1 4601 NM_005962.1 9,29 0,17	
0000 DOOM 1 000 A17	
205837_s_at GYPA 2993 BC005319.1 9,22 0,17	
208353_x_at ANK1 286 NM_020480.1 9,20 0,17	
202125_s_at ALS2CR3 66008 NM_015049.1 9,10 0,17	
20 217572_at AA654586 9,06 0,17	
211649_x_at L14456.1 9,04 0,17	
205838_at GYPA 2993 NM_002099.2 9,04 0,17	
202219_at SLC6A8 6535 NM_005629.1 9,03 0,17	
216925_s_at TAL1 6886 X51990.1 8,98 0,17	
25 203794_at CDC42BPA 8476 NM_014826.1 8,96 0,17	
211820_x_at GYPA 2993 U00179.1 8,95 0,17	
218864_at TNS 7145 AF116610.1 8,94 0,17	
215812_s_at U41163 8,90 0,17	
202074_s_at OPTN 10133 NM_021980.1 8,89 0,17	
30 201886_at WDR23 80344 NM_025230.1 8,86 0,17	
216833_x_at GYPE 2996 U05255.1 8,84 0,17	
202124_s_at ALS2CR3 66008 AV705253 8,84 0,17	
216317_x_at RHCE 6006 X63095.1 8,81 0,17	
204467_s_at SNCA 6622 NM_000345.2 8,80 0,17	
35 207087_x_at ANK1 286 NM_020478.1 8,78 0,17	
213843_x_at SLC6A8 6535 AW276522 8,78 0,17	
210586_x_at RHD 6007 AF312679.1 8,77 0,17	
209890_at TM4SF9 10098 AF065389.1 8,75 0,17	
218853_s_at DJ473B4 56180 NM_019556.1 8,74 0,17	
40 214433_s_at SELENBP1 8991 NM_003944.1 8,70 0,17	
48031_r_at C5orf4 10826 H93077 8,70 0,17	
208352_x_at ANK1 286 NM_020479.1 8,69 0,17	
203115_at FECH 2235 AU152635 8,66 0,17	

Table 31: Top40 genes of cluster #9

	Probe Set	Gene	Locus Link	Accession	Score	q-value SAM
	\mathbf{ID}	symbol	number	number	SAM	(%)
	201497_x_at	MYH11	4629	NM_022844.1	89,02	0,18
5	207961_x_at	MYH11	4629	NM_022870.1	26,72	0,18
	212358_at	CLIPR-59	25999	AL117468.1	20,92	0,18
	206135_at	ST18	9705	$NM_014682.1$	19,69	0,18
	212298_at	NRP1	8829	BE620457	18,71	0,18
	206682_at	CLECSF13	10462	NM_006344.1	15,32	0,18
10	203060_s_at	PAPSS2	9060	AF074331.1	15,04	0,18
	203058_s_at	PAPSS2	9060	AW299958	14,73	0,18
	205987_at	CD1C	911	$NM_001765.1$	12,82	0,18
	221019_s_at	COLEC12	81035	NM_030781.1	12,69	0,18
	204885_s_at	MSLN	10232	NM_005823.2	12,36	0,18
15	209396_s_at	CHI3L1	1116	M80927.1	12,06	0,18
	219694_at	FLJ11127	54491	NM_019018.1	11,59	0,18
	205076_s_at	CRA	10903	NM_006697.1	11,49	0,18
	209395_at	CHI3L1	1116	M80927.1	11,07	0,18
	219308_s_at	AK5	26289	NM_012093.1	10,88	0,18
20	207194_s_at	ICAM4	3386	NM_001544.2	10,76	0,18
	204787_at	Z39IG	11326	NM_007268.1	10,23	0,18
	200665_s_at	SPARC	6678	NM_003118.1	10,18	0,18
	201506_at	\mathbf{TGFBI}	7045	NM_000358.1	9,99	0,18
	212912_at	RPS6KA2	6196	AI992251	9,82	0,18
25	203939_at	NT5E	4907	NM_002526.1	9,67	0,18
	205330_at	MN1	4330	NM_002430.1	9,24	0,18
	202481_at	SDR1	9249	NM_004753.1	8,92	0,18
	212771_at	LOC221061	221061	AU150943	8,85	0,18
	210889_s_at	FCGR2B	2213	M31933.1	8,82	0,18
30	218876_at	CGI-38	51673	NM_016140.1	8,45	0,18
	203329_at	PTPRM	5797	NM_002845.1	8,25	0,18
	204197_s_at	RUNX3	864	NM_004350.1	-8,25	0,18
	200984_s_at	CD59	966	NM_000611.1	-8,33	0,18
	218414_s_at	NDE1	54820	NM_017668.1	-8,42	0,18
35	213779_at	EMU1	129080	AL031186	-8,56	0,18
	204198_s_at	RUNX3	864	AA541630	-8,85	0,18
	211026_s_at	MGLL	11343	BC006230.1	-9,01	0,18
	219218_at	FLJ23058	79749	NM_024696.1	-9,61	0,18
	206788_s_at	CBFB	865	AF294326.1	-9,73	0,18
40	218927_s_at	CHST12	55501	NM_018641.1	-9,82	0,18
	211031_s_at	CYLN2	7461	BC006259.1	-10,24	0,18
	202370_s_at	CBFB	865	NM_001755.1	-13,01	0,18
	200675_at	CD81	975	NM_004356.1	-14,28	0,18

Table 32: Top40 genes of cluster #10

	Probe Set	\mathbf{Gene}	Locus Link	Accession	Score	q-value SAM
	ID	symbol	number	number	SAM	(%)
	219145_at	FLJ11939	79732	NM_024679.1	12,59	0,21
5	202551_s_at	CRIM1	51232	BG546884	11,82	0,21
	47560_at	FLJ11939	79732	AI525402	11,75	0,21
	209763_at	NRLN1	91851	AL049176	8,99	0,21
	200671_s_at	SPTBN1	6711	NM_003128.1	8,75	0,21
	213488_at	FLJ00133	25992	AL050143.1	8,75	0,21
10	204004_at			AI336206	8,74	0,21
	205933_at	SETBP1	26040	NM_015559.1	8,63	0,21
	213506_at	F2RL1	2150	BE965369	8,53	0,21
	41577_at	PPP1R16B	26051	AB020630	8,52	0,21
	209679_s_at	LOC57228	57228	BC003379.1	8,51	0,21
15	212558_at	GDAP1L1	78997	BF508662	8,43	0,21
	207788_s_at	SCAM-1	10174	NM_005775.1	8,42	0,21
	204083_s_at	TPM2	7169	NM_003289.1	8,21	0,21
	209487_at	RBPMS	11030	$\overline{D84109.1}$	8,19	0,21
	207836_s_at	RBPMS	11030	NM_006867.1	8,14	0,21
20	209282_at	PRKD2	25865	AF309082.1	8,14	0,21
20	209436_at	SPON1	10418	AB018305.1	8,12	0,21
	204484_at	PIK3C2B	5287	NM_002646.1	8,11	0,21
	212750_at	PPP1R16B	26051	AB020630.1	8,09	0,21
	205330_at	MN1	4330	NM_002430.1	8,03	0,21
25	209576_at	GNAI1	2770	AL049933.1	8,02	0,21
	220377_at	C14orf110	29064	NM_014151.1_	7,91	0,21
-	203756_at	P164RHOGE		NM_014786.1	7,89	0,21
	200672_x_at	SPTBN1	6711	NM_003128.1	7,88	0,21
	212827_at	IGHM	3507	$X17\overline{1}15.1$	7,86	0,21
30	209437_s_at	SPON1	10418	AB051390.1	7,74	0,21
	204917_s_at	MLLT3	4300	AV756536	7,59	0,21
	204540_at	EEF1A2	1917	NM_001958.1	7,57	0,21
	208614_s_at	FLNB	2317	M62994.1	7,40	0,21
	204581_at	CD22	933	NM_001771.1_	7,29	0,21
35	218086_at	NPDC1	56654	NM_015392.1_	7,25	0,21
•	209488_s_at	RBPMS	11030	$D84\overline{109.1}$	7,21	0,21
	218899_s_at	BAALC	79870	NM_024812.1_	7,11	0,21
	203796_s_at	BCL7A	605	AI950380	7,05	0,21
	212071_s_at	SPTBN1	6711	BE968833	6,93	0,21
40	206111_at	RNASE2	6036	NM_002934.1	-7,00	0,21
	209906_at	C3AR1	719	U62027.1	-7,34	0,21
	205382_s_at	DF	1675	NM_001928.1_	-7,63	0,21
	214575_s_at	AZU1	566	NM_001700. 1 _	-7,95	0,21
		· ·		- ''		•

Table 33: Top40 genes of cluster #11

	Probe Set	Gene	Locus Link	Accession	Score	q-value SAM
	ID	symbol	number	number	SAM	(%)
_	209079_x_at	PCDHGC3	5098	AF152318.1	-2,72	1,48
5	207076_s_at	ASS	445	NM_000050.1	-2,74	1,48
	218825_at	EGFL7	51162	NM_016215.1	-2,74	1,48
	201522_x_at	SNRPN	6638	NM_003097.2	-2,74	1,48
	201601_x_at	IFITM1	8519	NM_003641.1	-2,75	1,48
	206042_x_at	SNRPN	6638	$NM_022804.1$	-2,80	1,48
10	209583_s_at	MOX2	4345	AF063591.1	-2,81	1,48
	204385_at	KYNU	8942	NM_003937.1	-2,84	1,48
	218805_at	IAN4L1	55340	NM_018384.1	-2,90	1,48
	214953_s_at	APP	351	X06989.1	-2,90	1,48
	203859_s_at	PALM	5064	NM_002579.1	-2,97	1,48
1 5	203542_s_at	BTEB1	687	BF438302	-2,97	1,48
	212171_x_at	VEGF	7422	H95344	-3,03	1,48
	218237_s_at	SLC38A1	81539	NM_030674.1	-3,05	1,48
	219777_at	hIAN2	79765	NM_024711.1	-3,07	1,48
	201656_at	ITGA6	3655	NM_000210.1	-3,13	1,48
20	208886_at	H1F0	3005	BC000145.1	-3,17	1,48
	203139_at	DAPK1	1612	NM_004938.1	-3,18	1,48
	31874_at	GAS2L1	10634	Y07846	-3,21	1,48
	218966_at	MYO5C	55930	NM_018728.1	-3,22	1,48
	216033_s_at	FYN	.2534	S74774.1	-3,23	1,48
25	218589_at	P2RY5	10161	NM_005767.1	-3,24	1,48
20	217838_s_at	EVL	51466	NM_016337.1	-3,25	1,48
	201279_s_at	DAB2	1601	BC003064.1	-3,26	1,48
	200762_at	DPYSL2	1808	NM_001386.1	-3,29	1,48
	209723_at	SERPINB9	5272	BC002538.1	-3,34	1,48
30	205125_at 205101_at	MHC2TA	4261	NM_000246.1	-3,37	1,48
50	208873_s_at	DP1	7905	BC000232.1	-3,43	1,48
	200075_s_at 211675_s_at	HIC	29969	AF054589.1	-3,49	1,48
	200665_s_at	SPARC	6678	NM_003118.1	-3,50	1,48
	213848_at	DUSP7	1849	AI655015	-3,54	1,48
35		DOSI 7 DNM1	1759	AF035321.1	-3,56	1,48
อย	215116_s_at	SIAT9	8869	NM_003896.1	-3,56	1,48
	203217_s_at	CD34	947	M81104.1	-3,57	1,48
	209543_s_at	ALDH2	217	NM_000690.1	-3,63	1,48
	201425_at		25932	AF109196.1	-4,00	1,48
40	201559_s_at	CLIC4		NM_013324.2	-4,36	1,48
40	221223_x_at	CISH	$1154 \\ 10184$	N66633	-4,43	1,48
	212658_at	LHFPL2		NM_002250.1	-4,43 -4,70	1,48
	204401_at	KCNN4	3783		-4,70 -4,95	1,48
	201560_at	CLIC4	25932	NM_013943.1	-4,50	1,40

Table 34: Top40 genes of cluster #12

ID		Probe Set		Locus Link	Accession	Score	q-value SAM
5 210998_s_at 205110_s_at 210794_s_at 204537_s_at 204537_s_at 204537_s_at 205614_x_at 205663_at 202260_s_at 202260_s_at 202260_s_at 203074_at 203074_at 204537_s_at 204537_s_at 205663_at 202260_s_at 203074_at 203074_at 203037_s_at 2030337_s_at 2030331_s_at 2030331_s_at 2030331_s_at 2030331_s_at 2030331_s_at 2030331_s_at 2030331_s_at 2030331_s_at 2030331_s_at 204152_				number	number	SAM	(%)
205110_s_at FGF13 2258 NM_004114.1 24,76 0,13 210794_s_at MEG3 55384 AFI19863.1 23,54 0,13 204587_s_at GABRE 2664 NM_004961.2 22,89 0,13 205614_x_at MST1 4485 NM_002098.1 20,74 0,13 20260_s_at STXBP1 6812 NM_0026528.1 20,42 0,13 216320_x_at MST1 4485 U37055 18,72 0,13 203074_at ANXA8 244 NM_001630.1 18,42 0,13 206663_at SIX3 6496 NM_0054613.1 16,41 0,13 216320_x_at MEG3 55384 A1950273 15,29 0,13 203397_s_at GALNT3 2591 BF063271 15,29 0,13 21732_at MEG3 55384 A1950273 15,24 0,13 207895_at ANALADASEL 10004 NM_005468.1 14,64 0,13 218048_s_at AZ2 64343 NM_002461.1 14,17 0,13 209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at PTGER1 5731 NM_000955.1 11,92 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 21668_s_at PTGDS 5730 M61900.1 11,44 0,13 214203_s_at PTGDS 5730 M61900.1 11,44 0,13 214203_s_at PTGDS 5730 M61900.1 11,33 0,13 21040_at CST7 S530 AF031824.1 11,27 0,13 200656_s_at P4HB 5034 NM_00295.1 11,24 0,13 200656_s_at P4HB 5034 NM_003489.1 11,35 0,13 200656_s_at P4HB 5034 NM_003489.1 11,27 0,13 200656_s_at P4HB 5034 NM_003489.1 11,24 0,13 200656_s_at P4HB 5034 NM_003489.1 11,24 0,13 200656_s_at P4HB 5034 NM_003489.1 11,57 0,13 200656_s_at P4HB 5034 NM_003489.1 11,57 0,13 200656_s_at P4HB 5034 NM_003489.1 11,57 0,13		210997_at					
210794_s_at MEG3 55384 AF119863.1 23,54 0,13 204537_s_at GABRE 2564 NM_004961.2 22,89 0,13 2066614_x_at MST1 4485 NM_020998.1 20,74 0,13 20260_s_at PCBP3 54039 NM_020528.1 20,42 0,13 202260_s_at STXBP1 6812 NM_003165.1 19,36 0,13 216320_x_at MST1 4485 U37055 18,72 0,13 203074_at ANXA8 244 NM_001630.1 18,42 0,13 206634_at SIX3 6496 NM_005413.1 16,41 0,13 203397_s_at GALNT3 2591 BF063271 15,29 0,13 212732_at MEG3 5584 A1950273 15,24 0,13 207895_at NAALADASEL 10004 NM_005468.1 14,64 0,13 208404_s_at AZ2 64343 NM_002461.1 14,17 0,13 209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at BF968134 12,27 0,13 212509_s_at BF968134 12,27 0,13 212204_at DKFZP664G2022 25963 AF182733.1 11,57 0,13 212204_at DKFZP664G2022 25963 AF182733.1 11,57 0,13 211663_x_at PTGDS 5730 M6190.1 11,44 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 200656_s_at P4HB 5034 NM_000948.1 11,26 0,13 200656_s_at P4HB 5034 NM_000948.1 11,26 0,13 200656_s_at P4HB 5034 NM_000948.1 11,27 0,13 200656_s_at P4HB 5034 NM_000948.1 11,23 0,13 200656_s_at P4HB 5034 NM_000948.1 11,26 0,13 200656_s_at P4HB 5034 NM_000948.1 11,26 0,13 200656_s_at P4HB 5034 NM_000948.1 11,33 0,13 200656_s_at P4HB 5034 NM_000948.1 11,26 0,13 200656_s_at P4HB 5034 NM_000948.1 11,33 0,13 200656_s_at P4HB 5034 NM_000948.2 11,12 0,13 204153_s_at NMEP1 S204 NM_0004348.2 11,12 0,13 204153_s_at NMEP1 S204 NM_0003930.1 -11,76 0,13 204362_at	5	210998_s_at	\mathbf{HGF}	3082		•	•
204537_s_at 206614_x_at MST1 4485 NM_004961.2 22,89 0,13 206614_x_at MST1 4485 NM_020998.1 20,74 0,13 20,6663_at PCBP3 54039 NM_020528.1 20,42 0,13 202260_s_at STXBP1 6812 NM_003165.1 19,36 0,13 216320_x_at MST1 4485 U37055 18,72 0,13 203074_at ANXA8 244 NM_001630.1 18,42 0,13 203074_at ANXA8 244 NM_001630.1 18,42 0,13 203074_at ANXA8 244 NM_001630.1 18,42 0,13 203397_s_at GALNT3 2591 BF063271 15,29 0,13 212732_at MEG3 55384 A1950273 15,24 0,13 212732_at MEG3 55384 A1950273 15,24 0,13 218043_s_at AZ2 64343 NM_022461.1 14,17 0,13 218043_s_at AZ2 64343 NM_022461.1 14,17 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at BF968134 12,27 0,13 212509_s_at PTGER1 5731 NM_000955.1 11,92 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 21663_x_at PTGDS 5730 M61900.1 11,33 0,13 200656_s_at P4HB 5034 NM_002025.1 11,27 0,13 200656_s_at P4HB 5034 NM_002045.1 11,24 0,13 200656_s_at P4HB 5034 NM_000343.2 11,12 0,13 200656_s_at NRIP1 8204 NM_00349.1 11,33 0,13 20140_at CST7 8530 AF031824.1 11,16 0,13 204362_at CALR 811 NM_004343.2 11,16 0,13 204362_at CALR 811 NM_003490.1 11,36 0,13 204362_at CALR 811 NM_003490.1 11,37 0,13 204362_at CALR 8204 NM_003489.1 11,36 0,13 204362_at CALR 8204 NM_003489.1 11,37 0,13 204362_at CALR 8204 NM_003489.1 11,36 0,13 204362_at CALR 8204 NM_003489.1 11,176 0,13 204362_at CALR		205110_s_at	FGF13	2258	NM_004114.1		
206614_x_st MST1		210794_s_at	MEG3	55384	AF119863.1		•
10 206663 at 202360 s. at 203360 s. at 3000 s. at 2033074 at 3000 s. at 3000 s. at 2033074 at 3000 s. at		204537_s_at	GABRE	2564	NM_004961.2	22,89	0,13
202260_s_at STXBP1 6812 NM_003165.1 19,36 0,13 216320_x_at MST1 4485 U37055 18,72 0,13 203074_at ANXA8 244 NM_001630.1 18,42 0,13 206634_at SIX3 6496 NM_005413.1 16,41 0,13 15 210755_at HGF 3082 U46010.1 16,11 0,13 203397_s_at GALNT3 2591 BF063271 15,29 0,13 212732_at MEG3 55384 AI950273 15,24 0,13 207895_at NAALADASEL 10004 NM_005468.1 14,64 0,13 218043_s_at AZ2 64343 NM_022461.1 14,17 0,13 209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 201276_at RAB5B 5869 AF267863.1 12,24 0,13 207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 207070_s_at LAMC1 3915 J03202.1 11,57 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 20654_at P4HB 5034 J02783.1 11,24 0,13 210656_s_at P4HB 5034 NM_000958.1 11,22 0,13 200656_s_at P4HB 5034 NM_0009443.2 11,12 0,13 200659_s_at CALR 811 NM_00443.2 11,12 0,13 200659_s_at NRIP1 8204 NM_00380.1 -11,76 0,13 204362_at SCAP2 8935 NM_00380.1 -11,76 0,13 204362_at CALR 811 NM_00380.1 -11,76 0,13 204362_s_at MRNG 4242 AI738965 -12,02 0,13 204362_s_at LGALS9 3965 NM_009587.1 -18,14 0,13 204362_s_at LGALS9 3965 NM_009587.1		205614_x_at	MST1	4485	NM_020998.1	20,74	0,13
202260_s_at MST1	10	205663_at	PCBP3	54039	NM_020528.1	20,42	0,13
216320_x_at			STXBP1	6812	NM_003165.1	19,36	0,13
203074_at ANXA8 244 NM_001630.1 18,42 0,13			MST1	4485	U37055	18,72	0,13
15			ANXA8	244	NM_001630.1	18,42	0,13
15 210755_at HGF 3082 U46010.1 16,11 0,13 203397_s_at GALNT3 2591 BF063271 15,29 0,13 212732_at MEG3 55384 A1950273 15,24 0,13 207895_at NAALADASEL 10004 NM_005468.1 14,64 0,13 218043_s_at AZ2 64343 NM_022461.1 14,17 0,13 209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at BF968134 12,27 0,13 207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 25 209960_at HGF 3082 X16323.1 11,57 0,13 212204_at DKF2P564G2022 25963 AF132733.1 11,57 0,13 207031_a			SIX3	6496	NM_005413.1	16,41	0,13
203397_s_at CALNT3 2591 BF063271 15,29 0,13 212732_at MEG3 55384 A1950273 15,24 0,13 207895_at NAALADASEL 10004 NM_005468.1 14,64 0,13 218043_s_at AZ2 64343 NM_022461.1 14,17 0,13 209961_s_at HGF 3082 M60718.1 13,51 0,13 209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at BF968134 12,27 0,13 207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 200770_s_at LAMC1 3915 J03202.1 11,57 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 20654_at P4HB 5034 NM_002025.1 11,28 0,13 21040_at CST7 8530 AF031824.1 11,16 0,13 21040_at CST7 8530 AF031824.1 11,16 0,13 204153_s_at MFNG 4242 NM_003489.1 -11,33 0,13 209336_s_at CALR 811 NM_003489.1 -11,33 0,13 200336_s_at NRIP1 8204 NM_003489.1 -11,57 0,13 204452_s_at MFNG 4242 NM_003930.1 -11,76 0,13 204452_s_at MFNG 4242 A1838965 -12,02 0,13 204153_s_at MFNG 4242 A1838965 -12,02 0,13 204152_s_at MFNG 4242 A1838965 -12,02 0,13 204153_s_at MFNG 4242 A1738965 -12,02 0,13 204152_s_at MFNG 4242 A173896	15			3082	U46010.1	16,11	0,13
212732_at MEG3 55384 AI950273 15,24 0,13					BF063271	15,29	0,13
207895_at NAALADASEL 10004 NM_005468.1 14,64 0,13 218043_s_at AZ2 64343 NM_022461.1 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,17 0,13 14,18 12,27 0,13 14,18 12,27 0,13 12,18 12,27 0,13 12,18 12,27 0,13 12,18 12,27 0,13 12,18 12,27 0,13 12,20 13 14,18 12,27 0,13 14,18 12,27 0,13 14,18 1					AI950273	15,24	0,13
218043_s_at				10004	NM_005468.1	14,64	
20 209961_s_at HGF 3082 M60718.1 13,51 0,13 209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at BF968134 12,27 0,13 207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 25 209960_at HGF 3082 X16323.1 11,88 0,13 200770_s_at LAMC1 3915 J03202.1 11,57 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 30 206105_at FMR2 2334 NM_002025.1 11,28 0,13 204656_s_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13		-			NM_022461.1	14,17	0,13
209815_at na 349352 U43148.1 12,71 0,13 201276_at RAB5B 5869 AF267863.1 12,44 0,13 212509_s_at BF968134 12,27 0,13 207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 20960_at HGF 3082 X16323.1 11,88 0,13 200770_s_at LAMC1 3915 J03202.1 11,57 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_00918.1 11,23 0,13 204153_s_at MFNG 4242 NM_0024343.2 11,12 0,13 204153_s_at NFNG	20				M60718.1	13,51	0,13
201276_at					U43148.1	12,71	0,13
212509_s_at BF968134 12,27 0,13 207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 25 209960_at HGF 3082 X16323.1 11,88 0,13 200770_s_at LAMC1 3915 J03202.1 11,57 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 30 206105_at FMR2 2334 NM_002025.1 11,28 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 20931_s_at VCL 7414 NM_014000.1 -11,57 0,13 20931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13		_			AF267863.1	12,44	0,13
207650_x_at PTGER1 5731 NM_000955.1 11,92 0,13 209960_at HGF 3082 X16323.1 11,88 0,13 200770_s_at LAMC1 3915 J03202.1 11,57 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 30 206105_at FMR2 2334 NM_002025.1 11,28 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 20931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13					BF968134	12,27	0,13
25			PTGER1	5731	NM_000955.1	11,92	0,13
200770_s_at LAMC1 3915 J03202.1 11,57 0,13 212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 30 206105_at FMR2 2334 NM_002025.1 11,28 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_003489.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,37 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 <tr< td=""><td>25</td><td></td><td></td><td></td><td></td><td>11,88</td><td>0,13</td></tr<>	25					11,88	0,13
212204_at DKFZP564G2022 25963 AF132733.1 11,55 0,13 207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 0,13 206105_at FMR2 2334 NM_002025.1 11,28 0,13 200654_at PAHB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 204153_s_at MFNG 4242 NM_002405.1 11,12 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13		_				11,57	0,13
207031_at BAPX1 579 NM_001189.1 11,44 0,13 211663_x_at PTGDS 5730 M61900.1 11,33 0,13 0,13 30 206105_at FMR2 2334 NM_002025.1 11,28 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 204153_s_at MFNG 4242 NM_004343.2 11,12 0,13 202599_s_at NRIP1 8204 NM_002405.1 -11,33 0,13 200931_s_at VCL 7414 NM_004400.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13				25963	AF132733.1	11,55	0,13
211663_x_at PTGDS 5730 M61900.1 11,33 0,13 206105_at FMR2 2334 NM_002025.1 11,28 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 20931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13		_			NM_001189.1	11,44	0,13
30 206105_at FMR2 2334 NM_002025.1 11,28 0,13 214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 20931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13					M61900.1	11,33	0,13
214203_s_at PRODH 5625 AA074145 11,27 0,13 200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13	30		FMR2	2334	NM_002025.1	11,28	0,13
200654_at P4HB 5034 J02783.1 11,24 0,13 200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13			PRODH	5625	AA074145	$11,\!27$	0,13
200656_s_at P4HB 5034 NM_000918.1 11,23 0,13 210140_at CST7 8530 AF031824.1 11,16 0,13 35 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13		200654_at	P4HB	5034	J02783.1	11,24	0,13
210140_at CST7 8530 AF031824.1 11,16 0,13 200935_at CALR 811 NM_004343.2 11,12 0,13 204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13			P4HB	5034	NM_000918.1	11,23	0,13
35			CST7	8530	AF031824.1	11,16	0,13
204153_s_at MFNG 4242 NM_002405.1 -11,33 0,13 202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13	35			811	NM_004343.2	11,12	0,13
202599_s_at NRIP1 8204 NM_003489.1 -11,33 0,13 200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13			MFNG	4242	NM_002405.1	-11,33	0,13
200931_s_at VCL 7414 NM_014000.1 -11,57 0,13 204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13			NRIP1	8204	NM_003489.1	-11,33	0,13
204362_at SCAP2 8935 NM_003930.1 -11,76 0,13 40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13			VCL	7414	NM_014000.1	-11,57	0,13
40 202600_s_at NRIP1 8204 AI824012 -11,86 0,13 204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13			SCAP2	8935	NM_003930.1	-11,76	0,13
204152_s_at MFNG 4242 AI738965 -12,02 0,13 203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13	40	-	NRIP1	8204	AI824012	-11,86	0,13
203236_s_at LGALS9 3965 NM_009587.1 -18,14 0,13					AI738965	-12,02	0,13
				3965	NM_009587.1	-18,14	0,13
				393	NM_001666.1	-21,49	0,13

Table 35: Top40 genes of cluster #13

	Probe Set		Locus Link	Accession	Score	q-value SAM
	\mathbf{ID}		number	number	SAM	(%)
	205529_s_at	CBFA2T1 (ETO)		$NM_004349.1$	60,36	0,14
5	205528_s_at	CBFA2T1 (ETO)		X79990.1	56,08	0,14
	216831_s_at	CBFA2T1 (ETO)) 862	AF018283.1	26,62	0,14
	213194_at	ROBO1	6091	BF059159	24,74	0,14
	204811_s_at	CACNA2D2	9254	NM_006030.1	23,53	0,14
	206940_s_at	POU4F1	5457	NM_006237.1	21,42	0,14
10	210744_s_at	IL5RA	3568	M75914.1	21,09	0,14
	211517_s_at	IL5RA	3568	M96651.1	20,92	0,14
	211341_at	POU4F1	5457	L20433.1	20,66	0,14
	204990_s_at	ITGB4	3691	NM_000213.1	20,55	0,14
	212097_at	CAV1	857	AU147399	20,47	0,14
15	216832_at	CBFA2T1	862	AF018283.1	17,51	0,14
	206128_at	ADRA2C	152	AI264306	16,87	0,14
	204874_x_at	BAIAP3	8938	NM_003933.2	16,41	0,14
	203065_s_at	CAV1	857	NM_001753.2	16,07	0,14
	212496_s_at	KIAA0876	23030	AW237172	15,75	0,14
20	212492_s_at	KIAA0876	23030	AW237172	15,66	0,14
	218613_at	DKFZp761K142		NM_018422.1	14,20	0,14
	206622_at	TRH	7200	NM_007117.1	13,63	0,14
	216356_x_at	BAIAP3	8938	AB018277.1	13,48	0,14
	201621_at	NBL1	4681	NM_005380.1	13,45	0,14
25	213894_at	LOC221981	221981	BF447246	13,05	0,14
	203088_at	FBLN5	10516	NM_006329.1	12,93	0,14
	204396_s_at	GPRK5	2869	NM_005308.1	12,66	0,14
	201655_s_at	HSPG2	3339	M85289.1	12,62	0,14
	218742_at	HPRN	64428	NM_022493.1	12,59	0,14
30	214920_at	LOC221981	221981	R33964	12,55	0,14
	219686_at	HSA250839	55351	NM_018401.1	12,44	0,14
	204073_s_at	C11orf9	745	NM_013279.1	12,35	0,14
	209822_s_at	VLDLR	7436	L22431.1	12,29	0,14
	206793_at	PNMT	5409	NM_002686.1	$12,\!27$	0,14
35	211685_s_at	NCALD	83988	AF251061.1	12,16	0,14
	214946_x_at	FLJ10824	55747	AV728658	12,03	0,14
	210010_s_at	SLC25A1	6576	U25147.1	11,84	0,14
	203741_s_at	ADCY7	113	NM_001114.1	-11,89	0,14
	208885_at	LCP1	3936	J02923.1	-12,03	0,14
40	204494_s_at	LOC56905	56905	AW516789	-12,21	0,14
	208091_s_at	DKFZP564K08	22 81552	NM_030796.1	-13,52	0,14
	220560_at	C11orf21	29125	NM_014144.1	-14,30	0,14
	221581_s_at	WBSCR5	7462	AF257135.1	-17,67	0,14

Table 36: Top 40 genes of cluster #14 (No significant genes identified.)

Table 37: Top 40 genes of cluster #15

5	Probe Set ID	Gene symbol	Locus Link number	Accession number	Score SAM	q-value SAM (%)
	206676_at	CEACAM8	1088	M33326.1	7,20	1,66
	204661_at	CDW52	1043	NM_001803.1	-3,44	1,07
	211182_x_at	RUNX1	861	AF312387.1	-3,46	1,07
10	212827_at	\mathbf{IGHM}	3507	X17115.1	-3,47	1,07
	203542_s_at	BTEB1	687	BF438302	-3,49	1,07
	214835_s_at	SUCLG2	8801	AF131748.1	-3,51	1,07
	209905_at	HOXA9	3205	AI246769	-3,56	1,07
	201867_s_at	TBL1X	6907	NM_005647.1	-3,59	1,07
15	204069_at	MEIS1	4211	NM_002398.1	-3,61	1,07
	205600_x_at	HOXB5	3215	AI052747	-3,62	1,07
	208962_s_at	FADS1	3992	BE540552	-3,63	1,07
	205453_at	HOXB2	$\bf 3212$	NM_002145.1	-3,69	1,07
	219256_s_at	FLJ20356	54436	NM_018986.1		1,07
20	218627_at	FLJ11259	55332	NM_018370.1	-3,76	1,07
	201719_s_at	EPB41L2	2037	NM_001431.1		1,07
	213150_at	HOXA10	3206	NM_018951.1		1,07
	209374_s_at	IGHM	3507	BC001872.1	-3,89	1,07
	210365_at	RUNX1	861	D43967.1	-3,90	1,07
25	214651_s_at	HOXA9	3205	U41813.1	-3,92	1,07
	218552_at	FLJ10948	55268	NM_018281.1	-3,94	1,07
	212906_at	na	283158	BE044440	-3,97	1,07
	213147_at	HOXA10	3206	NM_018951.1		1,07
	213400_s_at	TBL1X	6907	AV753028	-4,01	1,07
30	200765_x_at	CTNNA1	1495	NM_001903.1	-4,02	1,07
	202391_at	BASP1	10409	NM_006317.1	-4,07	1,07
	217226_s_at	PMX1	5396	M95929.1	-4,09	1,07
	217800_s_at	NDFIP1	80762	NM_030571.1		1,07
	201841_s_at	HSPB1	3315	$NM_001540.2$	•	1,07
35	202236_s_at	SLC16A1	6566	NM_003051.1		1,07
	212314 _at	KIAA0746	23231	AB018289.1	-4,43	1,07
	215772_x_at	SUCLG2	8801	AL050226.1	-4,44	1,07
	218847_at	IMP-2	10644	NM_006548.1		1,07
	212311_at	KIAA0746	23231	AB018289.1	-4,56	1,07
40	212459_x_at	SUCLG2	8801	BF593940	-4,63	1,07
	209191_at	TUBB-5	84617	BC002654.1	-4,63	1,07
	220974_x_at	BA108L7.2	81855	NM_030971.1		1,07
	217853_at	TEM6	64759	$NM_022748.1$		1,07
	$218501_{ m at}$	ARHGEF3	50650	NM_019555.1		1,07
45	40489_at	DRPLA	1822	D31840	-5,57	1,07
	221737_at	GNA12	2768	NM_007353.1	-5,84	1,07

Table 38: Top40 genes of cluster #16

	Probe Set	Gene	Locus Link	Accession	Score	q-value SAM
	ID	symbol	number	number	SAM	(%)
	220057_at	GAGED2	9503	NM_020411.1	22,48	0,27
5	219360_s_at	TRPM4	54795	NM_017636.1	21,22	0,27
	219414_{at}	CLSTN2	64084	NM_022131.1	16,98	0,27
	220116_at	KCNN2	3781	NM_021614.1	16,31	0,27
	216370_s_at	TKTL1	8277	Z49258	15,76	0,27
	205550_s_at	\mathbf{BRE}	9577	NM_004899.1	15,55	0,27
10	211566_x_at	BRE	9577	U19178.1	15,11	0,27
	214183_s_at	TKTL1	8277	X91817.1	14,70	0,27
	209031_at	IGSF4	23705	NM_014333.1	13,62	0,27
	212645_x_at	BRE	9577	AL566299	13,32	$0,\!27$
	209030_s_at	IGSF4	23705	NM_014333.1	13,30	0,27
15	213791_at	PENK	5179	NM_006211.1	13,25	0,27
	206508_at	TNFSF7	970	NM_001252.1	12,46	0,27
	219506_at	FLJ23221	79630	NM_024579.1	12,31	0,27
	211421_s_at	RET	5979	M31213.1	12,03	0,27
	203241_at	UVRAG	7405	NM_003369.1	11,99	0,27
20	213908_at	LOC339005	339005	AI824078	11,94	0,27
	207911_s_at	TGM5	9333	NM_004245.1	11,78	0,27
	214190_x_at	GGA2	23062	AI799984	11,49	0,27
	204561_x_at	APOC2	344	NM_000483.2	11,38	0,27
	209663_s_at	ITGA7	3679	AF072132.1	11,27	0,27
25	214259_s_at	AKR7A2	8574	AW074911	11,14	0,27
	205472_s_at	DACH	1602	NM_004392.1	10,91	0,27
	216331_at	ITGA7	3679	AK022548.1	10,89	0,27
	220010_at	KCNE1L	23630	NM_012282.1	10,78	0,27
	213484_at	na	151521	AI097640	10,73	0,27
30	204497_at	ADCY9	115	AB011092.1	10,48	0,27
	215771_x_at	RET	5979	X15786.1	10,33	0,27
	209032_s_at	IGSF4	23705	AF132811.1	10,32	0,27
	219714_s_at	CACNA2D3	55799	NM_018398.1	10,21	0,27
	219463_at	C20 or f103	24141	NM_012261.1	10,21	0,27
35	202139_at	AKR7A2	8574	NM_003689.1	9,87	0,27
	219143_s_at	FLJ20374	54913	$NM_017793.1$	9,66	0,27
	205996_s_at	AK2	204	NM_013411.1	9,60	0,27
	219288_at	HT021	57415	NM_020685.1	9,57	0,27
	215663_at	MBNL1	4154	BC005296.1	9,42	0,27
40	213361_at	PCTAIRE2BP	23424	AW129593	9,23	0,27
	210658_s_at	GGA2	23062	BC000284.1	8,73	0,27
	213772_s_at	GGA2	23062	BF196572	8,59	0,27
	212174_at	AK2	204	AK023758.1	8,59	0,27

Table 39: PAM genes of prognostically important clusters (#13, #12, #9, #16, #10, #4, #15, #4 and #15, and FLT3ITD)

5					
	Probe Set	Gene	Locus Link	Accession	Abnormality
	${ m ID}$	symbol	number	${f number}$	
	205529_s_at	ČBFA2T1 (ET	O)862	NM_004349.1	AML and $t(8;21)$
	205528_s_at	CBFA2T1 (ET		X79990.1	AML and t(8;21)
10	213194_at	ROBO1	6091	BF059159	AML and t(8;21)
	210997_at	\mathbf{HGF}	3082	M77227.1	AML and t(15;17)
	210998_s_at	\mathbf{HGF}	3082	M77227.1	AML and t(15;17)
	205110_s_at	FGF13	2258	NM_004114.1	AML and t(15;17)
	201497_x_at	MYH11	4629	$NM_022844.1$	AML and inv(16)
1 5	214183_s_at	TKTL1	8277	X91817.1	11q23 (cluster 16)
	216370_s_at	TKTL1	8277	Z49258	11q23 (cluster 16)
	220057_at	GAGED2	9503	NM_020411.1	11q23 (cluster 16)
	209031_at	IGSF4	23705	NM_014333.1	11q23 (cluster 16)
	209030_s_at	IGSF4	23705	NM_014333.1	11q23 (cluster 16)
20	219360_s_at	TRPM4	54795	NM_017636.1	11q23 (cluster 16)
	216331_at	ITGA7	3679	AK022548.1	11q23 (cluster 16)
	206508_at	TNFSF7	970	NM_001252.1	11q23 (cluster 16)
	204561_x_at	APOC2	344	NM_000483.2	11q23 (cluster 16)
	200989_at	HIF1A	3091	NM_001530.1	11q23 (cluster 16)
25	219506_at	FLJ23221	79630	$NM_024579.1$	11q23 (cluster 16)
	213791_at	PENK	5179	NM_006211.1	11q23 (cluster 16)
	205472_s_at	DACH	1602	NM_004392.1	11q23 (cluster 16)
	209629_s_at	NXT2	55916	AF201942.1	11q23 (cluster 16)
	219288_at	HT021	57415	NM_020685.1	11q23 (cluster 16)
30	205471_s_at	DACH	1602	$\overline{\mathrm{AW772082}}$	11q23 (cluster 16)
	219463_at	C20 or f103	24141	NM_012261.1	11q23 (cluster 16)
	209628_at	NXT2	55916	AK023289.1	11q23 (cluster 16)
	215571_at	to 101 101		AK021495.1	11q23 (cluster 16)
	209663_s_at	ITGA7	3679	AF072132.1	11q23 (cluster 16)
35	220010_at	KCNE1L	23630	NM_012282.1	11q23 (cluster 16)
	204885_s_at	MSLN	10232	NM_005823.2	11q23 (cluster 16)
	207911_s_at	TGM5	9333	NM_004245.1	11q23 (cluster 16)
	209032_s_at	IGSF4	23705	AF132811.1	11q23 (cluster 16)
	206277_at	P2RY2	5029	NM_002564.1	11q23 (cluster 16)
40	211421_s_at	RET	5979	M31213.1	11q23 (cluster 16)
	203241_at	UVRAG	7405	NM_003369.1	11q23 (cluster 16)
	209616_s_at	CES1	1066	S73751.1	11q23 (cluster 16)
	219714_s_at	CACNA2D3	55799	NM_018398.1	11q23 (cluster 16)
	213908_at	LOC339005	339005	AI824078	11q23 (cluster 16)
45	217520_x_at	na	219392	BG396614	11q23 (cluster 16)
	202551_s_at	CRIM1	51232	BG546884	EVI (cluster 10)
	213506_at	F2RL1	2150	BE965369	EVI (cluster 10)
	206111_at	RNASE2	6036	NM_002934.1	EVI (cluster 10)
	214575_s_at	AZU1	566	NM_001700.1	EVI (cluster 10)
50	209679_s_at	LOC57228	57228	BC003379.1	EVI (cluster 10)
	41577_at	PPP1R16B	26051	AB020630	EVI (cluster 10)
	212750_at	PPP1R16B	26051	AB020630.1	EVI (cluster 10)

Table 39: (continued)

	Probe Set	Gene	Locus Link	Accession	Abnormality	
	ID	symbol	number	number		
5	204540_at	EEF1A2	1917	$NM_001958.1$	EVI (cluster	10)
	205330_at	MN1	4330	$NM_002430.1$	EVI (cluster	10)
	200671_s_at	SPTBN1	6711	NM_003128.1	EVI (cluster	10)
	207788_s_at	SCAM-1	10174	NM_005775.1	EVI (cluster	10)
	209576_at	GNAI1	2770	AL049933.1	EVI (cluster	10)
10	218086_at	NPDC1	56654	NM_015392.1	EVI (cluster	10)
	204484_at	PIK3C2B	5287	NM_002646.1	EVI (cluster	10)
	219145_at	FLJ11939	79732	NM_024679.1	EVI (cluster	10)
	212820_at	RC3	23312	AB020663.1	EVI (cluster	10)
	204004at			AI336206	EVI (cluster	10)
15	209487_at	RBPMS	11030	D84109.1	EVI (cluster	10)
	209543_s_at	CD34	947	M81104.1	EVI (cluster	10)
	205382_s_at	\mathbf{DF}	1675	NM_001928.1	EVI (cluster	10)
	47560_at	FLJ11939	79732	AI525402	EVI (cluster	10)
	212827_at	IGHM	3507	X17115.1	EVI (cluster	10)
20	217977_at	SEPX1	51734	NM_016332.1	EVI (cluster	10)
	212558_at	GDAP1L1	78997	BF508662	EVI (cluster	10)
	206429_at	F2RL1	2150	NM_005242.2	EVI (cluster	10)
	220377_at	C14orf110	29064	NM_014151.1	EVI (cluster	10)
	206851_at	RNASE3	6037	NM_002935.1	EVI (cluster	10)
25	212012_at	D2S448	7837	AF200348.1	EVI (cluster	10)
	210844_x_at	CTNNA1	1495	D14705.1	cEBPalpha	(cluster 4)
	200765_x_at	CTNNA1	1495	NM_001903.1	cEBPalpha	(cluster 4)
	200764_s_at	CTNNA1	1495	AI826881	cEBPalpha	(cluster 4)
	214551_s_at	CD7	924	NM_006137.2	${\sf cEBPalpha}$	(cluster 4)
30	214049_x_at	CD7	924	AI829961	cEBPalpha	(cluster 4)
	216191_s_at	$\mathrm{TRD}@$	6964	X72501.1	cEBPalpha	(cluster 4)
	217143_s_at	TRD@	6964	X06557.1	cEBPalpha	(cluster 4)
	216286_at			AV760769	cEBPalpha	(cluster 4)
	206232_s_at	B4GALT6	9331	NM_004775.1	cEBPalpha	(cluster 4)
35	202241_at	C8FW	10221	NM_025195.1	${\sf cEBPalpha}$	(cluster 4)
	219383_at	FLJ14213	79899	NM_024841.1	cEBPalpha	(cluster 4)
	209191_at	TUBB-5	84617	BC002654.1	cEBPalpha	(cluster 4)
	213830_at	TRD@	6964	AW007751	cEBPalpha	(cluster 4)
	206676_at	CEACAM8	1088	M33326.1	${ m cEBPalpha}$	(cluster 15)
40	210244_at	CAMP	820	U19970.1	cEBPalpha	(cluster 15)
	202018_s_at	$_{ m LTF}$	4057	NM_002343.1	${ m cEBPalpha}$	(cluster 15)
	217853_at	TEM6	64759	NM_022748.1	c ${ m EBPalpha}$	(cluster 15)
	204417_at	GALC	2581	NM_000153.1	${ m cEBPalpha}$	(cluster 15)
	204039_at	CEBPA	1050	$NM_004364.1$	c ${ m EBPalpha}$	(cluster 15)
45	211810_s_at	GALC	2581	D25284.1	cEBPalpha	(cluster 15)
	210762_s_at	DLC1	10395	AF026219.1	cEBPalpha	(cluster 15)
	217800_s_at	NDFIP1	80762	NM_030571.1	${ m cEBPalpha}$	(cluster 15)
	206726_at	PGDS	27306	NM_014485.1	${ m cEBPalpha}$	(cluster 15)
	202236_s_at	SLC16A1	6566	NM_003051.1	${ m cEBPalpha}$	(cluster 15)
50	202016_at	MEST	4232	NM_002402.1	${ m cEBPalpha}$	(cluster 15)
	212531_at	LCN2	3934	NM_005564.1	cEBPalpha	(cluster 15)
	218847_at	IMP-2	10644	NM_006548.1	cEBPalpha	(cluster 15)

Table 39: (continued)

	Probe Set	Gene	Locus Link	Accession	n Abnormality	
5	ID	symbol	number	number		
	205692_s_at	CD38	952	NM_001775.1	cEBPalpha (cluster15)	
	212459_x_at	SUCLG2	8801	BF593940	cEBPalpha (cluster 15)	
	201841_s_at	HSPB1	3315	NM_001540.2	cEBPalpha (cluster15)	
	207329_at	MMP8	4317	NM_002424.1	cEBPalpha (cluster 15)	
10	220974_x_at	BA108L7.2	81855	NM_030971.1	cEBPalpha (cluster 15)	
10	207384_at	PGLYRP	8993	NM_005091.1	cEBPalpha (cluster 15)	
	209191_at	TUBB-5	84617	BC002654.1	cEBPalpha (cluster 15)	
	202391_at	BASP1	10409	NM_006317.1	cEBPalpha (cluster 15)	
	215772_x_at	SUCLG2	8801	AL050226.1	cEBPalpha (cluster15)	
4 ~	212314_at	KIAA0746	23231	AB018289.1	cEBPalpha (cluster15)	
15	221737_at	GNA12	2768	NM_007353.1	cEBPalpha (cluster 15)	
	214651_s_at	HOXA9	3205	U41813.1	cEBPalpha (cluster 15)	
	218501_at	ARHGEF3	50650	NM_019555.1	cEBPalpha (cluster15)	
20	202747_s_at	ITM2A	9452	NM_004867.1	cEBPalpha (cluster 15)	
	213400_s_at	TBL1X	6907	AV753028	cEBPalpha (cluster15)	
	214049_x_at	CD7	924	AI829961	cEBPalpha (cluster15)	
	209374_s_at	IGHM	3507	BC001872.1	cEBPalpha (cluster15)	
	212311_at	KIAA0746	23231	AB018289.1	cEBPalpha (cluster15)	
	40489_at	DRPLA	1822	D31840	cEBPalpha (cluster 15)	
05	205453_at	HOXB2	3212	NM_002145.1	cEBPalpha (cluster15)	
25	214551_s_at	CD7	924	NM_006137.2	cEBPalpha (cluster15)	
	206660_at	IGLL1	3543	NM_020070.1	cEBPalpha (cluster15)	
	210844_x_at	CTNNA1	1495	D14705.1	CEBPalpha (cluster 4 and 15)	
	200765_x_at	CTNNA1	1495	NM_001903.1	CEBPalpha (cluster 4 and 15)	
00	200764_s_at	CTNNA1	1495	AI826881	CEBPalpha (cluster 4 and 15)	
30	214551_s_at	CD7	924	NM_006137.2	CEBPalpha (cluster 4 and 15)	
	214049_x_at	CD7	924	AI829961	CEBPalpha (cluster 4 and 15)	
	209191_at	TUBB-5	84617	BC002654.1	CEBPalpha (cluster 4 and 15)	
	217800_s_at	NDFIP1	80762	NM_030571.1	CEBPalpha (cluster4 and 15)	
0.5	217143_s_at	TRD@	6964	X06557.1	CEBPalpha (cluster 4 and 15)	
35	216191_s_at	TRD@	6964	X72501.1	CEBPalpha (cluster 4 and 15)	
	219615_s_at	KCNK5	8645	NM_003740.1	FLT3 ITD	
	204341_at	TRIM16	10626	NM_006470.1	FLT3 ITD	
	201664_at	SMC4L1	10051	AL136877.1	FLT3 ITD	
40	201663_s_at	SMC4L1	10051	NM_005496.1	FLT3 ITD	
40	213110_s_at	COL4A5	1287	AW052179	FLT3 ITD	
	213844_at	HOXA5	3202	NM_019102.1	FLT3 ITD	
	204082_at	PBX3	5090	NM_006195.1	FLT3 ITD	
45	203151_at	MAP1A	4130	AW296788	FLT3 ITD	
	211269_s_at	IL2RA	3559	K03122.1	FLT3 ITD	
	203708_at	PDE4B	5142	NM_002600.1	FLT3 ITD	
	210425_x_at	GOLGIN-67	23015	AF164622.1	FLT3 ITD	
	212070_at	GPR56	9289	AL554008	FLT3 ITD	
	205366_s_at	HOXB6	3216	NM_018952.1	FLT3 ITD	
50	214039_s_at	LAPTM4B	55353	T15777	FLT3 ITD	
	203897_at	LOC57149	57149	BE963444	FLT3 ITD	
	215806_x_at	TRGC2	6967	M13231.1	FLT3 ITD	
	209813_x_at			M16768.1	FLT3 ITD	

Table 39: (continued)

	Probe Set	Gene	Locus Link	Accession	Abnorm	Abnormality	
5	${ m ID}$	symbol	number	number			
	216920_s_at	TRGC2	6967	M27331.1	FLT3	ITD	
	206945_at	LCT	3938	NM_002299.1	FLT3	ITD	
	208029_s_at	LAPTM4B	55353	NM_018407.1	FLT3	ITD	
	215288_at	TRPC2	7221	AI769824	FLT3	ITD	
10	203373_at	SOCS2	8835	$NM_003877.1$	FLT3	ITD	
	209905_at	HOXA9	3205	AI246769	FLT3	ITD	
	215623_x_at	SMC4L1	10051	AK002200.1	FLT3	ITD	
	211144_x_at	TRGC2	6967	M30894.1	FLT3	ITD	
	220813_at	CYSLTR2	57105	$NM_020377.1$	FLT3	ITD	
15	208767_s_at	LAPTM4B	55353	AW149681	FLT3	ITD	
	205227_at	IL1RAP	3556	$NM_002182.1$	FLT3	ITD	
	209014_at	MAGED1	9500	AF217963.1	FLT3	ITD	
	206341_at	IL2RA	3559	NM_000417.1	FLT3	ITD	
	205453_at	HOXB2	3212	$NM_002145.1$	FLT3	ITD	
20	209392_at	ENPP2	5168	L35594.1	FLT3	ITD	
	219304_s_at	SCDGF-B	80310	$NM_025208.1$	FLT3	ITD	
	208798_x_at	GOLGIN-67	23015	AF204231.1	FLT3	ITD	
	211302_s_at	PDE4B	$\boldsymbol{5142}$	L20966.1	FLT3	ITD	
	210839_s_at	ENPP2	5168	D45421.1	FLT3	ITD	
25	205600_x_at	HOXB5	3215	AI052747	FLT3	ITD	
	208414_s_at	HOXB4	3214	NM_002146.1	FLT3	ITD	
	208797_s_at	GOLGIN-67	23015	AI829170	FLT3	ITD	
	210123_s_at	CHRNA7	1139	U62436.1	FLT3	ITD	
	206289_at	HOXA4	3201	NM_002141.1	FLT3	ITD	
30	201069_at	MMP2	4313	NM_004530.1	FLT3	ITD	
	213217_at	ADCY2	108	AU149572	FLT3	ITD	
	214651_s_at	HOXA9	3205	U41813.1	FLT3	ITD	
	211402_x_at	NR6A1	2649	AF004291.1	FLT3	ITD	
	204044_at	QPRT	23475	NM_014298.2	FLT3	ITD	
35	204438_at	MRC1	4360	$NM_002438.1$	FLT3	ITD	
	206042_x_at	SNRPN	6638	NM_022804.1	FLT3	ITD	
	214953_s_at	APP	351	X06989.1	FLT3	ITD	
	201427_s_at	SEPP1	6414	NM_005410.1	FLT3	ITD	
	209193_at	PIM1	5292	M24779.1	FLT3	ITD	
40	219218_at	FLJ23058	79749	NM_024696.1	FLT3	ITD	
	200923_at	LGALS3BP	3959	NM_005567.2	FLT3	ITD	
	210424_s_at	GOLGIN-67	23015	AF163441.1	FLT3	ITD	
	219602_s_at	FLJ23403	63895	NM_022068.1	FLT3	ITD	
	201522_x_at	SNRPN	6638	NM_003097.2	FLT3	ITD	
45							